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DOD Hazardous Materials Information System
DoD 6050.5-L
AS OF July 1998

FSC: 6850
NIIN: 00F009088
Manufacturer's CAGE: SOUTH
Part No. Indicator: A
Part Number/Trade Name: 770836-FW836, MIL-C-38736

General Information

Item Name:
Company's Name: SOUTHWEST SOLV & CHEM
Company's Street: N/K
Company's P. O. Box: 41065
Company's City: HOUSTON
Company's State: TX
Company's Country:
Company's Zip Code: 77241
Company's Emerg Ph #: (713) 937-9300
Company's Info Ph #: (713) 937-9300
Distributor/Vendor # 1:
Distributor/Vendor # 1 Cage:
Distributor/Vendor # 2:
Distributor/Vendor # 2 Cage:
Distributor/Vendor # 3:
Distributor/Vendor # 3 Cage:
Distributor/Vendor # 4:
Distributor/Vendor # 4 Cage:
Safety Data Action Code:
Safety Focal Point: F
Record No. For Safety Entry: 001
Tot Safety Entries This Stk#: 001
Status:
Date MSDS Prepared: 07JUL88
Safety Data Review Date: 15AUG89
Supply Item Manager:
MSDS Preparer's Name:
Preparer's Company: SOUTHWEST SOLV & CHEM
Preparer's St Or P. O. Box: N/K
Preparer's City: HOUSTON
Preparer's State: TX
Preparer's Zip Code: 77241
Other MSDS Number:
MSDS Serial Number: BGZJR
Specification Number: MIL-C-38736
Spec Type, Grade, Class:
Hazard Characteristic Code:
Unit Of Issue:
Unit Of Issue Container Qty:
Type Of Container:
Net Unit Weight:

Report for NIIN: 00F009088

NRC/State License Number:
Net Explosive Weight:
Net Propellant Weight-Ammo:
Coast Guard Ammunition Code:

Ingredients/Identity Information

==========
Proprietary: NO
Ingredient: ETHYL ACETATE (SARA III)
Ingredient Sequence Number: 01
Percent: N/K
Ingredient Action Code:
Ingredient Focal Point: F
NIOSH (RTECS) Number: AH5425000
CAS Number: 141-78-6
OSHA PEL: 400 PPM
ACGIH TLV: 400 PPM; 9192
Other Recommended Limit: 400 PPM

Proprietary: NO
Ingredient: METHYL ETHYL KETONE (2-BUTANONE) (MEK) (SARA III)
Ingredient Sequence Number: 02
Percent: N/K
Ingredient Action Code:
Ingredient Focal Point: F
NIOSH (RTECS) Number: EL6475000
CAS Number: 78-93-3
OSHA PEL: 200 PPM/300 STEL
ACGIH TLV: 200 PPM/300STEL 9192
Other Recommended Limit: 590 MG/CUM

Proprietary: NO
Ingredient: TOLUENE (SARA III)
Ingredient Sequence Number: 03
Percent: N/K
Ingredient Action Code:
Ingredient Focal Point: F
NIOSH (RTECS) Number: XS5250000
CAS Number: 108-88-3
OSHA PEL: 200 PPM/150 STEL
ACGIH TLV: 50 PPM; 9293
Other Recommended Limit: 100 PPM

Proprietary: NO
Ingredient: XYLENES (O-,M-,P- ISOMERS) (SARA III)
Ingredient Sequence Number: 04
Percent: N/K
Ingredient Action Code:
Ingredient Focal Point: F
NIOSH (RTECS) Number: ZE2100000
CAS Number: 1330-20-7
OSHA PEL: 100 PPM/150 STEL
ACGIH TLV: 100 PPM/150STEL;9192

Report for NIIN: 00F009088

Other Recommended Limit: 100 PPM

Proprietary: NO
Ingredient: ALIPHATIC NAPHTHA
Ingredient Sequence Number: 05
Percent: N/K
Ingredient Action Code:
Ingredient Focal Point: F
NIOSH (RTECS) Number: 1002250AN
CAS Number: 64742898
OSHA PEL: 500 PPM

ACGIH TLV: 300 PPM
Other Recommended Limit: 100 PPM

Proprietary: NO
Ingredient: ISOPROPYL ALCOHOL (SARA III)
Ingredient Sequence Number: 06
Percent: N/K
Ingredient Action Code:
Ingredient Focal Point: F
NIOSH (RTECS) Number: NT8050000
CAS Number: 67-63-0
OSHA PEL: 400 PPM/500 STEL
ACGIH TLV: 400 PPM/500STEL;9192
Other Recommended Limit: 400 PPM

Proprietary: NO
Ingredient: ETHYL BENZENE (SARA III)
Ingredient Sequence Number: 07
Percent: N/K
Ingredient Action Code:
Ingredient Focal Point: F
NIOSH (RTECS) Number: DA0700000
CAS Number: 100-41-4
OSHA PEL: 100 PPM/125 STEL
ACGIH TLV: 100 PPM/125STEL 9192
Other Recommended Limit: 100 PPM
==========

Physical/Chemical Characteristics

==========
Appearance And Odor: CLEAR, WATER-WHITE KETONE
Boiling Point: 290F
Melting Point: N/R
Vapor Pressure (MM Hg/70 F): 40.9
Vapor Density (Air=1): 3.1
Specific Gravity: 60
Decomposition Temperature: N/R
Evaporation Rate And Ref: N/R
Solubility In Water: N/K
Percent Volatiles By Volume: 100%
Viscosity:
pH: N/R
Radioactivity:

Report for NIIN: 00F009088

Form (Radioactive Matl):
Magnetism (Milligauss):
Corrosion Rate (IPY): N/R
Autoignition Temperature:
==========

Fire and Explosion Hazard Data

==========
Flash Point: 18F
Flash Point Method: TCC
Lower Explosive Limit: 1.7%
Upper Explosive Limit: N/K
Extinguishing Media: NFPA CLASS B EXTINGUISHERS (CO2/FOAM) FOR CLASS 1B LIQUID FIRES.
Special Fire Fighting Proc: WATER SPRAY MAY BE INEFFECTIVE. DON'T ENTER CONFINED FIRE-SPACE W/O FULL BUNKER GEAR. USE FOG NOZZLES IF WATER IS USED. NIOSH APPROVED POSITIVE-PRESSURE SCBA.

Unusual Fire And Expl Hazrds: CLOSED CONTAINERS MAY EXPLODE IF EXPOSED TO EXTREME HEAT/HOT SURFACES/SPARKS/OPEN FLAME. VAPORS MAY IGNITE EXPLOSIVELY/ SPREAD LONG DISTANCES.

Reactivity Data

Stability: YES
Cond To Avoid (Stability): ISOLATE FROM OXIDIZERS, HEAT, SPARKS, OPEN FLAME, & HOT SURFACES.
Materials To Avoid: ISOLATE FORM STRONG OXIDIZERS SUCH AS PERMANGANATE, CHROMATE & PEROXIDES.
Hazardous Decomp Products: CO, CO2
Hazardous Poly Occur: NO
Conditions To Avoid (Poly): N/K

Health Hazard Data

LD50-LC50 Mixture: ORAL LD50 (RATS) 3000 MG/KG
Route Of Entry - Inhalation: YES
Route Of Entry - Skin: YES
Route Of Entry - Ingestion: YES
Health Haz Acute And Chronic: SKIN: IRRITATION, DEFATTING, DERMATITIS, REDNESS. EYES: TEARING, BLURRED VISION. INGESTION: HARMFUL/FATAL. ABDOMINAL IRRITATION, NAUSEA, VOMITING & DIARRHEA. INHALATION: IRRITATION.
Carcinogenicity - NTP: NO
Carcinogenicity - IARC: NO
Carcinogenicity - OSHA: NO
Explanation Carcinogenicity: NONE
Signs/Symptoms Of Overexp: INHALATION: IRRITATION. EYE/SKIN: IRRITATION. INESTION: HARMFUL/FATAL. STUDIES WITH LABORATORY ANIMALS INDICATES. THIS PRODUCT CAN CAUSE DAMAGE TO FETUS.
Med Cond Aggravated By Exp: PERSONS W/SEVERE SKIN, LIVER OR KIDNEY PROBLEMS SHOULD AVOID USE.
Emergency/First Aid Proc: SKIN: FLUSH W/PLENTY OF WATER. EYES: FLUSH W/PLENTY OF WATER FOR 15 MINUTES & GET MEDICAL ATTENTION. INHALATION: REMOVE TO FRESH AIR. IF BREATHING IS DIFFICULT GIVE OXYGEN. IF BREATHING HAS STOPPED GIVE ARTIFICIAL RESPIRATION. INGESTION: CALL PHYSICIAN

Report for NIIN: 00F009088

IMMEDIATELY. NEVER GIVE ANYTHING BY MOUTH TO AN UNCONSCIOUS PERSON.

Precautions for Safe Handling and Use

Steps If Matl Released/Spill: MOP UP W/ABSORBENT MATERIAL & TRANSFER TO HOOD. STOP SPILL AT SOURCE. DIKE AREA & CONTAIN. PUMP LIQUID TO SALVAGE TANK. REMAINDER MAY BE TAKEN UP ON ABSORBENT MATERIAL & SHOVELED INTO CONTAINERS.
Neutralizing Agent: N/R
Waste Disposal Method: DISPOSE OF REMAINDER BY LEGALLY APPLICABLE METHODS. RECYCLE/INCINERATE OBSERVING LOCAL, STATE & FEDERAL HEALTH SAFETY & POLLUTION LAWS.
Precautions-Handling/Storing: DON'T STORE >120F. AVOID FREE FALL OF LIQUID. GROUND CONTAINER FOR TRANSFERRING. WASH THOROUGHLY AFTER HANDLING. FOR INDUSTRY USE ONLY.
Other Precautions: KEEP OUT OF THE REACH OF CHILDREN. AVOID BREATHING VAPOR/SPRAY MIST/CONTACT W/SKIN & EYES. KEEP CONTAINER TIGHTLY CLOSED & UPRIGHT WHEN NOT IN USE TO PREVENT LEAKAGE. DON'T FLAME CUT, SAW, DRILL, BRAZE/WELD.

Control Measures

Respiratory Protection: VENTILATE TO KEEP AIR <90 PPM. USE A NIOSH APPROVED POSITIVE-PRESSURE SELF-CONTAINED BREATHING APPARATUS FOR EMERGENCIES.
Ventilation: MECHANICAL: ACCEPTABLE.
Protective Gloves: IMPERVIOUS
Eye Protection: GOGGLES, FACE SHIELD
Other Protective Equipment: APRON & FOOTWEAR IMPERVIOUS TO THIS MATERIAL. WASH CLOTHING BEFORE REUSE.
Work Hygienic Practices: WASH CLOTHING BEFORE REUSE. WASH THOROUGHLY AFTER HANDLING.
Suppl. Safety & Health Data: N/K

Transportation Data

Transportation Action Code:
Transportation Focal Point:
Trans Data Review Date:
DOT PSN Code:
DOT Symbol:
DOT Proper Shipping Name:
DOT Class:
DOT ID Number:
DOT Pack Group:
DOT Label:
DOT/DoD Exemption Number:
IMO PSN Code:
IMO Proper Shipping Name:
IMO Regulations Page Number:
IMO UN Number:
IMO UN Class:
IMO Subsidiary Risk Label:

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IATA PSN Code:
IATA UN ID Number:
IATA Proper Shipping Name:
IATA UN Class:
IATA Subsidiary Risk Class:
IATA Label:
AFI PSN Code:
AFI Symbols:
AFI Prop. Shipping Name:
AFI Class:
AFI ID Number:
AFI Pack Group:
AFI Label:
AFI Special Prov:
AFI Basic Pac Ref:
MMAC Code:
N.O.S. Shipping Name:
Additional Trans Data:

Disposal Data

Disposal Data Action Code:
Disposal Data Focal Point:
Disposal Data Review Date:
Rec # For This Disp Entry:
Tot Disp Entries Per NSN:

Landfill Ban Item:
Disposal Supplemental Data:
1st EPA Haz Wst Code New:
1st EPA Haz Wst Name New:
1st EPA Haz Wst Char New:
1st EPA Acute Hazard New:
2nd EPA Haz Wst Code New:
2nd EPA Haz Wst Name New:
2nd EPA Haz Wst Char New:
2nd EPA Acute Hazard New:
3rd EPA Haz Wst Code New:
3rd EPA Haz Wst Name New:
3rd EPA Haz Wst Char New:
3rd EPA Acute Hazard New:

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Label Data

==========

Label Required: YES
Technical Review Date:
Label Date:
MFR Label Number:
Label Status: G
Common Name: 770836-FW836, MIL-C-38736
Chronic Hazard: N/P
Signal Word:
Acute Health Hazard-None:
Acute Health Hazard-Slight:

Report for NIIN: 00F009088

Acute Health Hazard-Moderate:
Acute Health Hazard-Severe:
Contact Hazard-None:
Contact Hazard-Slight:
Contact Hazard-Moderate:
Contact Hazard-Severe:
Fire Hazard-None:
Fire Hazard-Slight:
Fire Hazard-Moderate:
Fire Hazard-Severe:
Reactivity Hazard-None:
Reactivity Hazard-Slight:
Reactivity Hazard-Moderate:
Reactivity Hazard-Severe:
Special Hazard Precautions: SKIN: IRRITATION, DEFATTING, DERMATITIS, REDNESS. EYES: TEARING, BLURRED VISION. INGESTION: HARMFUL/FATAL. ABDOMINAL IRRITATION, NAUSEA, VOMITING & DIARRHEA. INHALATION: IRRITATION. INHALATION: IRRITATION. EYE/SKIN: IRRITATION. INESTION: HARMFUL/FATAL. STUDIES WITH LABORATORY ANIMALS INDICATES. THIS PRODUCT CAN CAUSE DAMAGE TO FETUS.
Protect Eye:
Protect Skin:
Protect Respiratory:
Label Name: SOUTHWEST SOLV & CHEM
Label Street: N/K
Label P.O. Box: 41065
Label City: HOUSTON
Label State: TX
Label Zip Code: 77241
Label Country:
Label Emergency Number: 713) 937-9300

Year Procured:

ETHYL ACETATE (141-78-6)

summary from the About the Chemicals section of Scorecard

- **Human Health Hazards**

		Reference(s)
Recognized:	--	
Suspected:	Neurotoxicant	DAN RTECS
	Respiratory Toxicant	RTECS
	Skin or Sense Organ Toxicant	RTECS

- **Hazard Rankings**

  More hazardous than most chemicals in 3 out of 5 ranking systems.

- **Chemical Use Profile**

  This is a high volume chemical with production exceeding 1 million pounds annually in the U.S.
  Used in at least 6 industries.
  Used in consumer products, building materials or furnishings that contribute to indoor air pollution.

- **Profile of Environmental Release and Waste Generation**

  No data on environmental releases in Scorecard.

- **Regulatory Coverage**

  On at least 2 federal regulatory lists.

- **Basic Testing to Identify Chemical Hazards**

  2 of 8 basic tests to identify chemical hazards have not been conducted on this chemical, or are not publicly available.

- **Information Needed for Safety Assessment**

  Lacks at least some of the national data required for safety assessment.
  Scorecard has risk assessment data for this chemical.

- **Links**

  Other web sites specific to this chemical:

  - EPA Integrated Risk Information System Report
  - IPCS International Chemical Safety Card
  - International Toxicity Estimates for Risk (ITER) from the Toxicology Excellence for Risk Assessment
  - National Toxicology Program Health and Safety Information Sheet
  - New Jersey Fact Sheet

If none of these sources meet your needs, you can try searching some other chemical database Web sites.

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About the Chemicals

section of Scorecard

Chemical Profile Search

Scorecard provides detailed information on more than 6,800 chemicals, including all the chemicals used in large amounts in the United States and all the chemicals regulated under major environmental laws. You can search for information by typing in the chemical's name (or any common synonym) or the chemical's standard identification number (Chemical Abstracts Service or CAS registry number).

Name (or portion of name):

CAS number :

Rank Chemicals by Reported TRI Releases

For the 650 chemicals covered by the Toxics Release Inventory, Scorecard also lets you identify which are released or managed in the greatest quantity in your area. Scorecard tracks TRI chemicals using forty different ranking criteria, allowing you to select for chemicals in a specific TRI category (e.g, air releases), health effects category (e.g., air releases of recognized carcinogens), or risk-weighted category (e.g., ozone depleting potential).

Ranked by

Total environmental releases

in

Entire United States Go

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Scorecard

An information service provided by Environmental Defense

Scorecard News...

Pact with oil refiners will result in cleaner air in several states

A recent agreement reached with three petroleum refiners will reduce polluted air emissions from nine petroleum refineries in Delaware, Louisiana, Texas, California and Washington. Motiva Enterprises, Equilon Enterprises and Deer Park Refining arrived at a settlement with the Justice Department, the EPA and others to cut air pollutants by more than 60,000 tons per year.

The agreement addresses nitrogen oxides, sulfur dioxide and particulate emissions, which cause serious respiratory problems and exacerbate cases of childhood asthma. Toxic air pollutants produced in the refining process can cause cancer.

Read EPA press release

Take Action!

Ask President Bush to Fight Global Warming.

Setting Priorities

Want to know what the most important environmental problems in your community are? Scorecard lists the top ranking issues in your area, based on comparative risk projects.

Pollution Locator

Find out about the pollution problems in your community. Search by geographic area or company name, or explore our maps. Reports are currently available on water quality, criteria and hazardous air pollutants, toxic chemical releases from manufacturing plants, Superfund sites and other sources of land contamination, hazards from lead pollution, and animal waste produced by factory farms.

Pollution Rankings

Scorecard highlights pollution problems that put an area into the worst 20% of areas in the country, or in its own state, and spotlights the companies responsible.

About the Chemicals

Find out whether a chemical has been tested for health effects and how harmful it may be for you and the environment.

Health Effects

Select a health problem that concerns you and find out what chemicals are recognized or suspected causes.

Find Your Community

Just enter your zip code and find out what pollutants are being released into your community --and who is responsible.

Go

Explore Maps

Air

- Criteria Air Pollutants
- Hazardous Air Pollutants

Land

- Superfund Sites and Potential Sources of Land Contamination
- Lead Hazards

Waste

- Animal Wastes from Factory Farms
- Toxic Chemical Releases from Manufacturing Facilities

Water

- Clean Water Act Status
- Watershed Indicators

Scorecard Top Ten

Counties in the U.S. with Superfund sites

1. SANTA CLARA, CA
2. LOS ANGELES, CA
3. MONTGOMERY, PA
4. BURLINGTON, NJ
5. NASSAU, NY
6. MIDDLESEX, MA
7. MIDDLESEX, NJ
8. CHESTER, PA
9. SUFFOLK, NY

Regulatory Controls

Find out about the regulatory programs that govern chemicals.

Discussion Forums

Share your views about pollution problems in your community, agricultural pollution, chemicals in consumer products, or the health effects of chemicals.

Take Action

Get the real story on toxics in your community and organize a community meeting on toxics using Scorecard's Guide. Scorecard lets you send faxes--for free--straight to the top-ranked polluters in your area or send email to key state and federal decision makers. We provide a directory of environmental organizations in your area and link you directly to volunteer opportunities with groups working on your issues. Or you can support Scorecard by running banners, distributing our data or maps, or contributing to Environmental Defense.

10. HARRIS, TX

Search Scorecard

Go

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- About Scorecard

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Email questions regarding the data or
how to use this information to protect the environment.

About the Chemicals: Data Descriptions

in the About the Chemicals section of Scorecard

Human Health Hazards

Exposure to toxic chemicals can cause any of several negative effects on human health, such as cancer or birth defects. Scorecard highlights the specific health hazards that each particular chemical poses. Twelve separate categories of health effects are covered. Some chemicals are widely recognized to be hazardous, while others are only suspected, so Scorecard always distinguishes between "recognized" and "suspected" health threats.

Hazard Rankings

Toxic chemicals can pose threats in many ways. How bad a particular chemical is depends on whether you are most concerned about its effects on humans, or its persistence in the environment, its damaging effects on ecosystems, or another factor. Scorecard shows how a chemical stacks up comparatively under different ranking systems. It then spotlights the chemicals that are most dangerous to human health and to the environment.

Chemical Use Profile

Why is industry using a toxic chemical in the first place? Scorecard uses official U.S. EPA information to tell you what each chemical is used for in various industries. If a chemical contributes to indoor air pollution, Scorecard points out the types of consumer products it may be found in. It also tells you if a chemical is one of the most widespread chemicals in commercial use (that is, an industrial chemical with annual U.S. production of more than one million pounds).

Profile of Releases and Waste Generation by Industrial Sector

What types of industries are responsible for releasing a particular chemical to the environment or for generating the greatest amount of chemical waste? Based on company reports to the EPA Toxics Release Inventory, Scorecard shows you the manufacturing sectors that release the largest quantities of a particular chemical or that generate the largest quantities as production-related waste.

Regulatory Coverage

Is government doing anything to control a toxic chemical? Scorecard tells you if a chemical is covered by federal environmental laws, or by California state laws (because California has unusually effective and innovative laws such as Proposition 65). It also tells you what chemicals are major environmental hazards because they damage the ozone layer, contribute to global warming, or persist in the environment.

Basic Testing to Identify Chemical Hazards

If an industrial chemical is allowed by law to be released into the environment, most people assume that it must have been tested and evaluated for its potential risks. Unfortunately, this is simply not true. Keeping chemical hazards under control requires information about what kinds of hazards each chemical poses. If the basic tests to check on a chemical's toxicity haven't been conducted, or if the results aren't publicly available, current laws tend to treat that chemical as if it were perfectly safe. For the chemicals being used in large quantities, Scorecard tells you whether or not eight basic types of tests for health and ecological effects have actually been conducted, based on the public record.

Information Needed for Safety Assessment

Could government assess a chemical's safety or risk? For most of the important industrial chemicals in U.S. commerce, government lacks the information to draw any scientifically based conclusion about the degree of risk--or lack of risk--that a chemical may pose when used. For every chemical in the database, Scorecard tells you whether or not the information needed to assess chemical risk is available. If it isn't, no one can accurately claim the chemical is "safe."

The key information for assessing a chemical's risk. To be able to assess the risk or safety of a chemical being released into the environment, two different kinds of information are needed: how toxic the chemical is, and how much people are actually being exposed to the chemical. For each chemical, Scorecard tells you whether or not there are risk assessment values (measuring its toxicity) available from the U.S. EPA or other authoritative scientific and regulatory agencies, and if so, what the values are. Scorecard also tells you whether information about human exposure to the chemical is being collected by national monitoring programs. Scorecard also directs you to sources of information about chemical contamination in your area.

Links

To make it easier to get more information on the hazards posed by a particular chemical, Scorecard points you to other web sites that provide publicly accessible fact sheets and other detailed technical information on chemicals. If there is a major toxicological profile of a chemical available online, it is rarely more than a click away.

Chemical Classes Scorecard tracks the classes that chemicals belong to and tells you which chemicals are members of which class. If you can't find something about one specific chemical, Scorecard can lead you to related chemicals for which more information may be available.

Other Web Sites Scorecard provides links to other database-backed web sites for further online research into chemical hazards.

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Neurotoxicity Definition

from the Health Effects section of Scorecard

Neurotoxicity is defined as adverse effects on the structure or functioning of the central and/or peripheral nervous system that result from exposure to chemical substances. Neurotoxicants can cause morphological changes that lead to generalized damage to nerve cells (neuronopathy), injury to axons (axonopathy), or destruction of the myelin sheath (myelinopathy). It is well established that exposure to certain agricultural and industrial chemicals can damage the nervous system, resulting in neurological and behavioral dysfunction. Symptoms of neurotoxicity include muscle weakness, loss of sensation and motor control, tremors, alterations in cognition, and impaired functioning of the autonomic nervous system

The central nervous system (CNS) is composed of the brain and spinal cord. It is responsible for the higher functions of the nervous system (conditioned reflexes, learning, memory, judgment, and other functions of the mind). Chemicals toxic to the CNS can induce confusion, fatigue, irritability, and other behavioral changes. Methyl mercury and lead are known CNS toxicants. Exposure to these metals can also cause degenerative diseases of the brain (encephalopathy).

The peripheral nervous system (PNS) includes all the nerves not in the brain or spinal cord. These nerves carry sensory information and motor impulses. Damage to the nerve fibers of the PNS can disrupt communication between the CNS and the rest of the body. The organic solvents carbon disulfide, n-hexane,and trichloroethylene can harm the PNS, resulting in weakness in the lower limbs, prickling or tingling in the limbs (paresthesia), and loss of coordination.

Exposure to chemical agents can trigger a wide range of adverse effects on the nervous system. Neurotoxic substances can alter the propagation of nerve impulses or the activity of neurotransmitters and can disrupt the maintenance of the myelin sheath or the synthesis of protein. As a result, neurotoxicological assessments require the administration of a battery of functional and observational tests. Neurotoxicity in humans is most commonly measured by neurological tests that assess cognitive, sensory, and motor function.

For further general information on chemicals and neurotoxicity, see the following references:

International Programme on Chemical Safety (IPCS). Principles and Methods for the Assessment of Neurotoxicity Associated with Exposure to Chemicals. Environmental Health Criteria, no. 60. Geneva: World Health Organization, 1986.

Needleman, H. L. Behavioral Toxicology. Environmental Health Perspectives. 103(Supplement 6): 77-79. 1995.

Norton, S. Toxic Responses of the Central Nervous System. Chapter 13 in Casarett and Doull's Toxicology, edited by C. Klaassen, M. Amdur, and J. Doull. New York: Pergamon Press, 1996.

Office of Technology Assessment. Neurotoxicity: Identifying and Controlling Poisons of the Nervous System. Washington, D.C.: Government Printing Office, 1990.

More

- references used to compile the list of neurotoxicants
- list of neurotoxicants

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Neurotoxicity References

from the Health Effects section of Scorecard

There is no generally accepted source for an authoritative list of chemicals that are recognized to cause neurotoxicity.

EDF's list of suspect neurotoxicants is compiled from the following sources:

AEGL: US EPA, National Advisory Committee for Acute Exposure Guideline Levels for Hazardous Substances. Notices. 62 Federal Register: 58839-58851 (October 30, 1997).

CAA-AQC: US Environmental Protection Agency, Office of Research and Development. Air Quality Criteria for Carbon Monoxide. Washington, DC, December 1991.

CAPCOA: California Environmental Protection Agency and California Air Pollution Control Officers Association. Air Toxics Hotspots Program Risk Assessment Guidance: Revised 1992 Risk Assessment Guidance and Draft Evaluation of Acute Non-Cancer Health Effects. Office of Environmental Health Hazard Assessment, CalEPA, Berkeley, CA. December 1994 and January 1995. http://www.oehha.org/air/hot_spots/index.html

CARB-TAC: California Air Resources Board. Toxic Air Contaminant Identification List Summaries and Proposed Update to the Toxic Air Contaminant List. Air Resources Board, CalEPA, Sacramento, CA. January 1996 and December 1998. http://www.arb.ca.gov/toxics/tac/tac.htm.

DAN: Nordic Council of Ministers and Danish National Institute of Occupational Health. Neurotoxic Substances in the Working Environment (Danish ad hoc list). List originally published in Neurotoxic Substances in the Work Environment, Danish Working Environment Service, At-report Nr. 13/1990. Suspect neurotoxicity identification now incorporated into 1998 Danish EPA All Chemicals List. http://www.mst.dk/udgiv/publications/2000/87-7909-501-1/pdf/87-7909-500-3.pdf.

EDF: See EDF's Custom Hazard Identification documentation.

EPA-HEN: US Environmental Protection Agency. Health Effects Notebook for Hazardous Air Pollutants. Review Draft. December 1994. http://www. epa.gov/ttn/uatw/hapindex.html

EPA-SARA: Roadmaps to Sources of Information on Chemicals Listed in the Emergency Planning Community and Community Right-to-Know Act (Also Known as SARA Title 3), Section 313 Toxic Release Inventory (for Microcomputers). (Report Number EPADFDK92040). 1991. Data file distributed in 2 diskettes by Office of Pollution, Prevention, and Toxics, Environmental Protection Agency, Washington, DC. NOTE: Datasource no longer being maintained by EPA; not currently available online.

EPA-TRI: US Environmental Protection Agency. Addition of Certain Chemicals; Toxic Chemical Release Reporting; Community Right to Know. Proposed and Final Rules. 59 Federal Register 1788 (Jan 12, 1994); 59 Federal Register 61432 (November 30, 1994).

EVAN: Evangelista, A.M. Behavioral Toxicology, Risk Assessment, and Chlorinated Hydrocarbons. Environmental. Health Perspectives. 104 (Supplement 2): 353-360. 1996. (Table 1: Comparison of behavioral toxicity of chlorinated hydrocarbons and related compounds).

FELD: Feldman, R.G. Role of the Neurologist in Hazard Identification and Risk Assessment. Environmental Health Perspectives. 104 (Supplement 2):227-237. 1996. (Table 1: Neurologic symptoms and associated exposures).

HEAST: EPA, Office of Research and Development. Health Effects Assessment Summary Tables. Electronic Handbook of Risk Assessment Values 9(6):6/30/00. Electronic Handbook Publishers, Redmond, WA. http://www.wolfenet.com/~sdwyer/ehrav.htm

KLAA: Klaassen, C., M. Amdur and J. Doull (eds.). Casarett and Doull's Toxicology. The Basic Science of Poisons, 5th Ed. Pergamon Press, NY. 1996. (Tables 16-1: Compounds Associated with Neuronal Injury, Table 16-2: Compounds Associated with Axonal Injury, Table 16-3: Compounds Associated with Injury of Myelin).

LU: Lu, F.C. Basic Toxicology. 2nd Edition. 1991. (Appendix 16-1: Selected Neurotoxicants).

MASL: Massachusetts Department of Public Health. Commonwealth of Massachusetts. 105CMR 670.000 Administrative Bulletin Concerning Massachusetts Substance List for "Right to Know" Law, M.G.L. 111F. 4/24/93. (Appendix A: Massachusetts Substance List)

NJ-FS: New Jersey Department of Health Services. Right to Know Program, NJDOH, Trenton, NJ. http://www.state.nj.us/health/eoh/rtkweb/

OEHHA-2000: Office of Environmental Health Hazard Assessment, California Environmental Protection Agency. Air Toxics Hot Spots Program Risk Assessment Guidelines, Part III. February, 2000 (http://www.oehha.ca.gov/air/chronic_rels/22RELS2k.html) and May, 2000 (http://www.oehha.ca.gov/air/chronic_rels/42kChREL.html)

OEHHA-99: Office of Environmental Health Hazard Assessment, California Environmental Protection Agency. Air Toxics Hot Spots Program Risk Assessment Guidelines, Part III, Draft Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels. June 1999 (http://www.oehha.ca.gov/air/chronic_rels/RAGSII.html) and October, 1999 (http://www.oehha.ca.gov/air/chronic_rels/RAGSp3draft.html).

OEHHA-97: Office of Environmental Health Hazard Assessment, California Environmental Protection Agency. Draft Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels. October 1997. http://www.oehha.org/air/chronic_rels/GETRELS.html

RTECS: National Institute for Occupational Safety and Health's Registry of Toxic Effects of Chemical Substances. See EDF's Suspect Hazard Identification documentation.

STAC: Stacey, N.H. Occupational Toxicology. Taylor & Francis. 1995. (Table 3.9: Occupational diseases - brain and spinal cord, Table 3.10: Occupations associated with an excess of brain cancer, Table 3.11: Agents capable of producing brain cancer in experimental animals, Table 3.12: Occupational diseases - mental disorders, Table 3.14: Agents causing occupational neuropathy).

TANN: Tanner, C. Occupational and Environmental Causes of Parkinsonism. Occupational Medicine 7(3): 5-3-513. (Table 2: Occupational and Environmental Causes of Parkinsonism).

ZAKR: Zakrzewski, S.F. Principles of Environmental Toxicology. American Chemical Society,

Washington, DC. 1997. (Table 7.4: TLV-TWA Values of Some Neurotoxins).

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- definition of neurotoxicity
- list of neurotoxicants

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Respiratory Toxicity Definition

from the Health Effects section of Scorecard

Respiratory toxicity is defined as adverse effects on the structure or functioning of the respiratory system that result from exposure to chemical substances. The respiratory tract consists of the nasal passages, pharynx, trachea, bronchi, and lungs. The chief function of the respiratory system is to ensure the efficient and effective exchange of oxygen and carbon dioxide between the blood and the air. Respiratory toxicants can produce a variety of acute and chronic pulmonary conditions, including local irritation, bronchitis, pulmonary edema, emphysema, and cancer.

It is well known that exposure to environmental and industrial chemicals can impair respiratory function. The air we breathe may contain toxic gases, vapors from solvents, aerosols, or particulate matter, all of which can cause respiratory harm. For example, scientific evidence has shown that ozone and fine particles pose a significant threat to respiratory health. Ground-level ozone, the main component in smog, causes breathing problems, aggravates asthma, and increases the severity and incidence of respiratory infections. More rarely, toxicants such as the herbicide paraquat may affect the respiratory tract after ingestion or dermal exposure.

Acute exposure to respiratory toxicants can trigger effects ranging from mild irritation to death by asphyxiation. Prolonged exposure to respiratory toxicants can cause structural damage to the lungs, resulting in chronic diseases such as pulmonary fibrosis, emphysema, and cancer. Pulmonary fibrosis is a serious lung disease in which airways become restricted or inflamed, leading to loss of elasticity and difficulty in breathing. It can be caused by exposure to coal dust, aluminum, beryllium, and carbides of tungsten. Emphysema, a degenerative and potentially fatal disease, is characterized by the inability of the lungs to fully expand and contract. The most common cause of emphysema is heavy cigarette smoking, but the disease can also be induced by exposure to aluminum, cadmium oxide, ozone, and nitrogen oxides. In addition, several toxicants are known to cause respiratory cancer. Examples of well-established human lung carcinogens are cigarette smoke, asbestos, arsenic, and nickel.

For further general information on chemicals and respiratory toxicity, see the following references:

Menzel, D. B.,and M. Amdur. Toxic Responses of the Respiratory System. Chapter 15 in Casarett and Doull's Toxicology, edited by C. Klaassen, M. Amdur, and J. Doull. New York: Pergamon Press, 1996.

Schlesinger, R. B., and J. Graham. Health Effects of Atmospheric Acid Aerosols: A Model Problem in Inhalation Toxicology and Air Pollution Risk Assessment (Symposium Overview). Fundamental and Applied Toxicology. 18: 17-24. 1992.

Vallyathan, V.,and X. Shi. The Role of Oxygen Free Radicals in Occupational and Environmental Lung Disease. Environmental Health Perspectives. 105(Supplement 1): 165-177. 1997.

More

- references used to compile the list of respiratory toxicants
- list of respiratory toxicants

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Respiratory Toxicity References

from the Health Effects section of Scorecard

There is no generally accepted source for an authoritative list of chemicals that are recognized to cause respiratory toxicity.

EDF's list of suspect respiratory toxicants is compiled from the following sources:

AEGL: US EPA, National Advisory Committee for Acute Exposure Guideline Levels for Hazardous Substances. Notices. 62 Federal Register: 58839-58851 (October 30, 1997).

CAA-AQC: US Environmental Protection Agency, Office of Research and Development. Air Quality Criteria for Ozone and Related Photochemical Oxidants, Volume III Washington, DC. July 1996.
US Environmental Protection Agency, Office of Research and Development. Air Quality Criteria for Oxides of Nitrogen, Volume III Washington, DC. August 1993.
US Environmental Protection Agency, Office of Research and Development. Air Quality Criteria for Particulate Matter and Sulfur Oxides, Volume III Washington, DC. December 1982.
US Environmental Protection Agency, Office of Research and Development. Air Quality Criteria for Particulate Matter, Volume III Washington, DC. April 1996.

CAPCOA: California Environmental Protection Agency and California Air Pollution Control Officers Association. Air Toxics Hotspots Program Risk Assessment Guidance: Revised 1992 Risk Assessment Guidance and Draft Evaluation of Acute Non-Cancer Health Effects. Office of Environmental Health Hazard Assessment, CalEPA, Berkeley, CA. December 1994 and January 1995. http://www.oehha.org/air/hot_spots/index.html

CARB-TAC: California Air Resources Board. Toxic Air Contaminant Identification List Summaries and Proposed Update to the Toxic Air Contaminant List. Air Resources Board, CalEPA, Sacramento, CA. January 1996 and December 1998. http://www.arb.ca.gov/toxics/tac/tac.htm

EDF: See EDF's Custom Hazard Identification documentation.

EEC: European Economic Community. Sensitizing Substances in the EEC List of Dangerous Substances. Annex I to Council Directive 67/548/EEC.

EPA-HEN: US Environmental Protection Agency. Health Effects Notebook for Hazardous Air Pollutants. Review Draft. December 1994. http://www.epa.gov/ttn/uatw/hapindex.html

EPA-TRI: US Environmental Protection Agency. Addition of Certain Chemicals; Toxic Chemical Release Reporting; Community Right to Know. Proposed and Final Rules. 59 Federal Register 1788 (Jan 12, 1994); 59 Federal Register 61432 (November 30, 1994).

FOTH: Foth, H. Role of the Lung in Accumulation and Metabolism of Xenobiotic compounds-Implications for Chemically Induced Toxicity. Critical Reviews in Toxicology. 25(2): 165- 205. 1995. (Table 1:Toxic Damage of Lung by Foreign Compounds).

KLAA: Klaassen, C., M. Amdur and J. Doull (eds.). Casarett and Doull's Toxicology. The Basic Science of Poisons, 5th Ed. Pergamon Press, NY. 1996. (Table 15-1: Industrial Toxicants that Produce Lung

Disease).

LADO: LaDou, J. (ed.). Occupational Medicine. Appleton & Lange, Norwalk, CT. 1990. (Table 39-1: Major pollutants associated with adverse pulmonary effects).

LU: Lu, F.C. Basic Toxicology. 2nd Edition. 1991. (Appendix 11-1: Site of Action and Pulmonary Disease Produced by Selected Occupationally Inhaled Toxicants).

NEME: Nemery, B. Metal Toxicity and the Respiratory Tract. European Respiratory Journal. 3(2): 202-219. 1990.(Table 1: Summary of pulmonary toxicity of metals).

NJ-FS: New Jersey Department of Health Services. Right to Know Program, NJDOH, Trenton, NJ. http://www.state.nj.us/health/eoh/rtkweb/

NTP-HS: National Toxicology Program. Chemical Repository of Health and Safety Data. http://ntp-db.niehs.nih.gov/NTP_Reports/NTP_Chem_H&S/NTP_Chem8/Radian85-01- 8.txt

OEHHA-2000: Office of Environmental Health Hazard Assessment, California Environmental Protection Agency. Air Toxics Hot Spots Program Risk Assessment Guidelines, Part III. February, 2000 (http://www.oehha.ca.gov/air/chronic_rels/22RELS2k.html) and May, 2000 (http://www.oehha.ca.gov/air/chronic_rels/42kChREL.html)

OEHHA-99: Office of Environmental Health Hazard Assessment, California Environmental Protection Agency. Air Toxics Hot Spots Program Risk Assessment Guidelines, Part III, Draft Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels. June 1999 (http://www.oehha.ca.gov/air/chronic_rels/RAGSII.html) and October, 1999 (http://www.oehha.ca.gov/air/chronic_rels/RAGSp3draft.html).

OEHHA-97: Office of Environmental Health Hazard Assessment, California Environmental Protection Agency. Draft Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels. October 1997. http://www.oehha.org/air/chronic_rels/GETRELS.html

OEHHA-AREL: Office of Environmental Health Hazard Assessment, California Environmental Protection Agency. All acute reference exposure levels developed by OEHHA as of May 2000. May, 2000. http://www.oehha.org/air/acute_rels/allAcRELs.html

RTECS: National Institute for Occupational Safety and Health's Registry of Toxic Effects of Chemical Substances. See EDF's Suspect Hazard Identification documentation.

More

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- list of respiratory toxicants

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Skin or Sense Organ Toxicity Definition

from the Health Effects section of Scorecard

Skin and sense organ toxicity is defined as adverse effects on the skin or sense organs that result from exposure to chemical substances. The senses of smell, vision, hearing, and taste are referred to as the special senses. Sense organs may be injured by a variety of physical, chemical, and biological agents. The sense of smell can become impaired, for example, as a result of occupational exposure to the metals cadmium and nickel. A variety of chemicals that act both locally and systemically in the body can affect vision. Airborne chemicals such as inorganic irritant gases and vapors (ammonia, chlorine, hydrogen sulfide, and sulfur dioxide) formaldehyde, and many organic solvents can cause external eye irritation, including conjunctivitis and keratitis, in some cases reducing visual acuity. Chemical substances can induce auditory dysfunction as well. Occupational exposure to lead, for example, is associated with hearing loss.

The skin provides the body with a protective barrier, contains the nerves that support the sense of touch, and participates in the exchange of gases and liquids. When the skin is exposed to irritant compounds, symptoms of skin injury may occur: redness, inflammation, burning, and itching. Acute and chronic skin diseases that may result from contact with toxic agents include dermatitis, photosensitization, chloracne, urticaria, and cancer.

One of the most common chemically induced skin disorders is contact dermatitis, an inflammatory reaction of the skin that is usually restricted to the exposed areas. Clinical signs may include reddening, edema, itching, or a burning sensation. Strongly alkaline and acidic substances such as sodium hydroxide, sulfuric acid, and hydrofluoric acid are some of the irritants that can cause contact dermatitis and related disorders. A number of skin toxicants produce photosensitization, an abnormal reaction to ultraviolet and/or visible radiation. Known photosensitizers include anthraquinone dyes, sulfanilamide, and coal tar derivatives (anthracene, pyridine, acridine, and phenanthrene). Chloracne is a severe and unusual form of acne that can be triggered by exposure to certain halogenated aromatic compounds, such as polychlorinated dibenzo furans and dioxins. Finally, arsenic, coal tars, creosote oils, and ultraviolet light have been shown to induce skin cancer in humans.

For further general information on chemicals and skin and sense organ toxicity, see the following references:

Adams, R. M. Occupational Skin Disease. 2 nd ed. Philadelphia: Saunders, 1990.

Emmett, E. A. Toxic Responses of the Skin. Chapter 15 in Casarett and Doull's Toxicology, edited by C. Klaassen, M. Amdur, and J. Doull. New York: Pergamon Press, 1996.

Kimmel, C. A. Dermal Toxicology. Archives of Toxicology. Supplement 15: 123-129. 1992.

Potts, A. Toxic Responses of the Eye. Chapter 17 in Casarett and Doull's Toxicology, edited by C. Klaassen, M. Amdur, and J. Doull. New York: Pergamon Press, 1996.

Shusterman, D. J., and J. Sheedy. Occupational and Environmental Disorders of the Special Senses. Occupational Medicine. 7(3): 515-542. 1992.

More

- references used to compile the list of skin or sense organ toxicants
- list of skin or sense organ toxicants

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Skin or Sense Organ Toxicity References

from the Health Effects section of Scorecard

There is no generally accepted source for an authoritative list of chemicals that are recognized to cause skin or sensory organ toxicity.

EDF's list of suspect skin or sensory organ toxicants is compiled from the following sources:

AEGL: US EPA, National Advisory Committee for Acute Exposure Guideline Levels for Hazardous Substances. Notices. 62 Federal Register: 58839-58851 (October 30, 1997).

CARB-TAC: California Air Resources Board. Toxic Air Contaminant Identification List Summaries and Proposed Update to the Toxic Air Contaminant List. Air Resources Board, CalEPA, Sacramento, CA. January 1996 and December 1998. http://www.arb.ca.gov/toxics/tac/tac.htm.

EDF: See EDF's Custom Hazard Identification documentation.

EEC: European Economic Community. Sensitizing Substances in the EEC List of Dangerous Substances. Annex I to Council Directive 67/548/EEC.

EPA-HEN: US Environmental Protection Agency. Health Effects Notebook for Hazardous Air Pollutants. Review Draft. December 1994. http://www. epa.gov/ttn/uatw/hapindex.html

EPA-TRI: US Environmental Protection Agency. Addition of Certain Chemicals; Toxic Chemical Release Reporting; Community Right to Know. Proposed and Final Rules. 59 Federal Register 1788 (Jan 12, 1994); 59 Federal Register 61432 (November 30, 1994).

HARV: Harvell, J., M. Bason and H. Maibach. Contact Urticaria and its Mechanisms. Food Chemistry and Toxicology 32(2): 103-112. 1994. (Table 2: Substances identified as capable of causing contact urticaria).

KLAA: Klaassen, C., M. Amdur and J. Doull (eds.). Casarett and Doull's Toxicology. The Basic Science of Poisons, 5th Ed. Pergamon Press, NY. 1996. (Tables 18-2: Selected Chemicals Causing Skin Burns, Table 18-3: Common Contact Allergens, Table 18- 6: Selected Phototoxic Agents, Table 18-8: Causes of Chloracne).

LADO: LaDou, J. (ed.). Occupational Medicine. Appleton & Lange, Norwalk, CN. 1990. (Table 17-1: Occupational phototoxic dermatitis: Causes and workers affected, Table 17-4: Common causes of occupational allergic contact dermatitis and typical occupational groups affected, Table 17-5: Established causes of occupational vitiligo, Table 17-8: Occupational cutaneous carcinogens and occupations with significant exposure).

LOCK: Lock, E.A., and E. Harpur. Toxicology of Sensory System: A Perspective. Human and Experimental Toxicology. 11(6): 442-448. 1992. (Table 1: Chemicals that induce olfactory lesions in experimental animals by either inhalation and/or non- inhalation routes).

LU: Lu, F.C. Basic Toxicology. Fundamentals, Target Organs, and Risk Assessment. 2nd Ed. 1991. (Appendix 15-1: Cataractogenic Chemicals).

NJ-FS: New Jersey Department of Health Services. Right to Know Program, NJDOH, Trenton, NJ. http://www.state.nj.us/health/eoh/rtkweb/

NTP-HS: National Toxicology Program. Chemical Repository of Health and Safety Data. http://ntp-db.niehs.nih.gov/NTP_Reports/NTP_Chem_H&S/NTP_Chem8/Radian85 -01-8.txt

OOEHHA-2000: Office of Environmental Health Hazard Assessment, California Environmental Protection Agency. Air Toxics Hot Spots Program Risk Assessment Guidelines, Part III. February, 2000 (http://www.oehha.ca.gov/air/chronic_rels/22RELS2k.html) and May, 2000 (http://www.oehha.ca.gov/air/chronic_rels/42kChREL.html)

OEHHA-99: Office of Environmental Health Hazard Assessment, California Environmental Protection Agency. Air Toxics Hot Spots Program Risk Assessment Guidelines, Part III, Draft Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels. June 1999 (http://www.oehha.ca.gov/air/chronic_rels/RAGSII.html) and October, 1999 (http://www.oehha.ca.gov/air/chronic_rels/RAGSp3draft.html).

OEHHA-97: Office of Environmental Health Hazard Assessment, California Environmental Protection Agency. Draft Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels. October 1997. http://www.oehha.org/air/chronic_rels/GETRELS.html

OEHHA-AREL: Office of Environmental Health Hazard Assessment, California Environmental Protection Agency. All acute reference exposure levels developed by OEHHA as of May 2000. May, 2000. http://www.oehha.org/air/acute_rels/allAcRELs.html

RTECS: National Institute for Occupational Safety and Health's Registry of Toxic Effects of Chemical Substances. See EDF's Suspect Hazard Identification documentation.

TIMB: Timbrell, J.A. Introduction to Toxicology. Taylor and Francis, New York. 1995. (Table 5.1: Types of skin sensitizers).

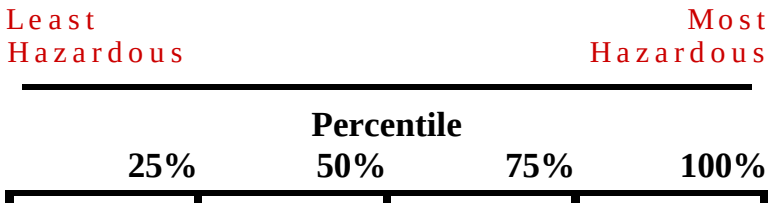
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- list of skin or sense organ toxicants

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Hazard Rankings

for ETHYL ACETATE (141-78-6) from Scorecard



Human Health Rankings

Toxicity and exposure potential

- Noncancer Risk Score - Air Releases (EDF)
- Noncancer Risk Score - Water Releases (EDF)
- Worker Exposure Hazard Score (IRCH)

Ecological Health Rankings

Toxicity and persistence

- Environmental Hazard Value Score (IRCH)

Integrated Environmental Rankings

Combined human and ecological scores

- Total Hazard Value Score (IRCH)

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High Production Volume (HPV) Chemicals

from Scorecard

DESCRIPTION

High production volume chemicals have annual production and/or importation volumes above 1 million pounds. In the U.S., 2,979 chemicals (excluding polymers) out of approximately 70,000 chemicals in commerce are used in such substantial quantities. While there are no authoritative estimates of the amount of total chemical use in the U.S., 4.4 to 7.1 trillion pounds of HPV chemicals are produced/imported annually.

The Organization for Economic Co-operation and Development (OECD) also maintains a list of 4,102 HPV chemicals. The OECD list includes chemicals which have annual production volumes greater than 1 thousand metric tonnes (2.2 million pounds) in more than one economically developed country.

REFERENCES

The U.S. list of HPV chemicals was generated from company reports of chemical use in 1990, submitted in response to the Toxic Substances Control Act Inventory Update Rule. Companies are only required to report their chemical production/imports as a range. The EPA is currently working on updating their HPV list using 1994 inventory reports.

Note that chemicals used as pesticides, food additive, drugs and cosmetics are not included in EPA's HPV list.

EPA's High Production Volume Chemical List
http://www.epa.gov/opptintr/chemrtk/hpvchmlt.htm

OECD's High Production Volume Chemical List
http://www.oecd.org/ehs/hpv.htm

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Industrial Uses

for ETHYL ACETATE (141-78-6) from Scorecard

This is a high volume chemical with production exceeding 1 million pounds annually in the U.S.

Which Industries Use This Chemical?	How is the Chemical Used in This Industry?
Electroplating	Electroplating - Vapor Degreasing Solvents
Laboratory Chemicals	Solvents - Dilution
Laboratory Chemicals	Solvents - Extraction
Paint Manufacture	Solvents, Not Elsewhere Classified
Printing	Solvents for Flexography
Printing	Solvents for Gravure Printing
Semiconductors	Developers - Positive
Wood Stains and Varnishes	Varnish Solvents

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Consumer Products

that contain ETHYL ACETATE (141-78-6) from Scorecard

What kinds of consumer products may contain this chemical?

- Aerosol paint concentrates
- Auto, other transportation, and machinery refinish paints incl primers
- Gravure inks
- Lubricating oils
- Misc. use aromatics
- Miscellaneous paint-related products
- Moisturizing creams
- Nail enamel and polish removers
- Nail enamels and polishes
- Nonstructural caulking compounds and sealants
- Other automotive chemicals
- Other gravure inks
- Other indust. product finishes excl. pigment dispersions & ink vehicles
- Other manicuring preparations
- Packaging inks: solvent types
- Packaging inks: solvent types
- Paint thinners
- Peripheral computer equipment
- Premoistened towelettes, incl wipes for babies
- Shoe polishes and cleaners
- Specialty performance sealants
- Synthetic resin and rubber adhesives

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Regulatory Coverage

of ETHYL ACETATE (141-78-6) from Scorecard

Federal Regulatory Program Lists

- Air Contaminants (Occupational and Safety Health Act)
- Hazardous Substances (Superfund)

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Basic Testing to Identify Chemical Hazards

for ETHYL ACETATE (141-78-6) from Scorecard

The U.S. EPA conducted a comprehensive review of publicly available chemical testing data in 1997 to examine whether the basic information needed to identify chemical hazards is available for high production volume chemicals. EPA searched major chemical databases to determine if the following tests had been conducted on a chemical:

- Acute toxicity
- Chronic toxicity
- Neurotoxicity
- Developmental or reproductive toxicity
- Mutagenicity
- Carcinogenicity
- Ecotoxicity
- Environmental fate

The following basic tests to identify chemical hazards have either not been conducted or are not publicly available:

- Carcinogenicity
- Chronic toxicity

More on the importance of basic toxicity testing

Reference

EPA. Chemical Hazard Data Availability Study: High Production Volume (HPV) Chemicals and SIDS Testing
Office of Pollution Prevention and Toxics, EPA,Washington, DC. 1998.

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Safety Assessment Data

for ETHYL ACETATE (141-78-6) from Scorecard

Are Risk Assessment Values Available?

Health Risk of Concern	Inhalation	Ingestion
Cancer	Not a recognized carcinogen	Not a recognized carcinogen
Noncancer	**No**	Yes

Are Exposure Data Available?

Type of Exposure	
Inhalation - ambient air	**No**
Inhalation - indoor air	**No**
Ingestion	**No**

- See the data US EPA possesses for safety assessment.

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Scorecard Risk Characterization Data

for ETHYL ACETATE (141-78-6) from Scorecard

Risk Assessment Values or Standards

	Value	Units	Reference
Inhalation cancer risk value (potency)	Not a recognized or suspect carcinogen		
Inhalation noncancer risk value (reference concentration)	Data gap		
National ambient air quality standard	Gap in regulatory coverage		
Ingestion cancer risk value (potency)	Not a recognized or suspect carcinogen		
Ingestion noncancer risk value (reference dose)	0.9	mg/kg-day	IRIS-HEAST
National water quality standard	Gap in regulatory coverage		

See the data US EPA possesses for safety assessment.

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Ethyl acetate

CASRN 141-78-6

Contents

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I.B. REFERENCE CONCENTRATION FOR CHRONIC INHALATION EXPOSURE (RfC)

II. CARCINOGENICITY ASSESSMENT FOR LIFETIME EXPOSURE

VI. BIBLIOGRAPHY

VII. REVISION HISTORY

VIII. SYNONYMS

0157
Ethyl acetate; CASRN 141-78-6

Health assessment information on a chemical substance is included in IRIS only after a comprehensive review of chronic toxicity data by U.S. EPA health scientists from several Program Offices and the Office of Research and Development. The summaries presented in Sections I and II represent a consensus reached in the review process. Background information and explanations of the methods used to derive the values given in IRIS are provided in the Background Documents.

STATUS OF DATA FOR Ethyl acetate

File On-Line 03/31/1987

Category (section)	Status	Last Revised
Oral RfD Assessment (I.A.)	on-line	03/01/1988
Inhalation RfC Assessment (I.B.)	no data	

Carcinogenicity Assessment (II.) no data

_I. CHRONIC HEALTH HAZARD ASSESSMENTS FOR NONCARCINOGENIC EFFECTS

__I.A. REFERENCE DOSE FOR CHRONIC ORAL EXPOSURE (RfD)

Substance Name -- Ethyl acetate
CASRN -- 141-78-6
Last Revised -- 03/01/1988

The oral Reference Dose (RfD) is based on the assumption that thresholds exist for certain toxic effects such as cellular necrosis. It is expressed in units of mg/kg-day. In general, the RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. Please refer to the Background Document for an elaboration of these concepts. RfDs can also be derived for the noncarcinogenic health effects of substances that are also carcinogens. Therefore, it is essential to refer to other sources of information concerning the carcinogenicity of this substance. If the U.S. EPA has evaluated this substance for potential human carcinogenicity, a summary of that evaluation will be contained in Section II of this file.

___I.A.1. ORAL RfD SUMMARY

Critical Effect	Experimental Doses*	UF	MF	RfD
Mortality and body weight loss	NOEL: 900 mg/kg/day LOAEL: 3600 mg/kg/day	1000	1	9E-1 mg/kg/day
Rat Oral Subchronic Study				
U.S. EPA, 1986				

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*Conversion Factors: none

I.A.2. PRINCIPAL AND SUPPORTING STUDIES (ORAL RfD)

U.S. EPA. 1986. Rat oral subchronic study with ethyl acetate. Office of Solid Waste, Washington, DC.

Ethyl acetate is fairly nontoxic [LD50 orally in rats: 11.3 g/kg, (Smyth et al., 1962)] and because of its characteristic fruity odor and pleasant taste when diluted, it is primarily used as fruit essences. Pertinent information regarding the mutagenicity, teratogenicity and carcinogenicity of ethyl acetate could not be located in the available literature. Therefore, the U.S. EPA, Office of Solid Waste, under the RCRA Land Disposal Ban, sponsored the 90-day subchronic study of ethyl acetate with rats. Four groups of rats (30/sex/group) were gavaged daily with 0, 300, 900 and 3600 mg/kg/day of ethyl acetate. Six weeks after the initial dosing, 10 rats/sex were subjected to interim sacrifice while the remaining rats continued on the dosing regimen until the final sacrifice (90 days). This study generated data on weekly body weights and food consumption, clinical signs of toxicity, ophthalmological evaluations, moribundity, mortality, blood and urine chemistry and gross and histopathologic evaluations of target organs. Evaluation of the data indicated that male rats exposed to the high dose (3600 mg/kg/day) of ethyl acetate showed significant toxic effects, which resulted in depressed body and organ weights, and depressed food consumption. Female rats exposed to the high dose showed slight but nonsignificant depression of above parameters compared with controls. The next lower dose (900 mg/kg/day) did not produce any adverse effects in either male or female rats and is, therefore, considered a NOEL. By applying an uncertainty factor of 1000 to this NOEL of 900 mg/kg/day, an RfD of 0.9 mg/kg/day or 63 mg/day for a 70-kg person can be recommended.

I.A.3. UNCERTAINTY AND MODIFYING FACTORS (ORAL RfD)

UF -- An uncertainty factor of 1000 is applied: 10 for intra- and 10 for interspecies extrapolation, and 10 to extrapolate subchronic to chronic exposure.

MF -- None

I.A.4. ADDITIONAL COMMENTS (ORAL RfD)

None.

___I.A.5. CONFIDENCE IN THE ORAL RfD

Study -- High
Data Base -- Low
RfD -- Low

The principal study is a well-designed oral study that includes several toxicologic endpoints; high confidence in the study is recommended. The data base did not provide information on additional subchronic/chronic or reproductive toxicity studies; therefore, low confidence is recommended. Confidence in the RfD can be considered low to medium.

___I.A.6. EPA DOCUMENTATION AND REVIEW OF THE ORAL RfD

Source Document -- U.S. EPA, 1987

Other EPA Documentation -- U.S. EPA, 1986

Agency Work Group Review -- 06/11/1986

Verification Date -- 06/11/1986

___I.A.7. EPA CONTACTS (ORAL RfD)

Please contact the Risk Information Hotline for all questions concerning this assessment or IRIS, in general, at (513)569-7254 (phone), (513)569-7159 (FAX) or RIH.IRIS@EPAMAIL.EPA.GOV (internet address).

__I.B. REFERENCE CONCENTRATION FOR CHRONIC INHALATION EXPOSURE (RfC)

Substance Name -- Ethyl acetate
CASRN -- 141-78-6

Not available at this time.

_II. CARCINOGENICITY ASSESSMENT FOR LIFETIME EXPOSURE

Substance Name -- Ethyl acetate
CASRN -- 141-78-6

This substance/agent has not undergone a complete evaluation and determination under US EPA's IRIS program for evidence of human carcinogenic potential.

_VI. BIBLIOGRAPHY

Substance Name -- Ethyl acetate
CASRN -- 141-78-6
Last Revised -- 08/01/1989

__VI.A. ORAL RfD REFERENCES

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U.S. EPA. 1986. Rat oral subchronic study with ethyl acetate. Office of Solid Waste, Washington, DC.

U.S. EPA. 1987. Health and Environmental Effects Profile for Ethyl Acetate. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste and Emergency Response, Washington, DC.

__VI.B. INHALATION RfD REFERENCES

None

__VI.C. CARCINOGENICITY ASSESSMENT REFERENCES

None

_VII. REVISION HISTORY

Substance Name -- Ethyl acetate
CASRN -- 141-78-6

Date	Section	Description
08/01/1989	VI.	Bibliography on-line
01/01/1992	I.A.7.	Primary contact changed
01/01/1992	IV.	Regulatory actions updated
04/01/1997	III.,IV., V.	Drinking Water Health Advisories, EPA Regulatory Actions, and Supplementary Data were removed from IRIS on or before April 1997. IRIS users were directed to the appropriate EPA Program Offices for this information.

VIII. SYNONYMS

Substance Name -- Ethyl acetate
CASRN -- 141-78-6
Last Revised -- 03/31/1987

141-78-6
ACETIC ACID, ETHYL ESTER
ACETIC ETHER
ACETIDIN
ACETOXYETHANE
AETHYLACETAT
ESSIGESTER
ETHYLACETAAT
Ethyl Acetate
ETHYL ACETIC ESTER
ETHYLE (ACETATE D')
ETHYL ETHANOATE
ETILE (ACETATO DI)
OCTAN ETYLU
RCRA WASTE NUMBER U112
UN 1173
VINEGAR NAPHTHA
.

IRIS Home Page | Substance File List

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Last updated: **5 May 1998**
URL: http://www.epa.gov/iris/subst/0157.htm

International Chemical Safety Cards

ETHYL ACETATE

ICSC: 0367

ETHYL ACETATE
Acetic acid, ethyl ester
Acetic ether
$C_4H_8O_2$ / $CH_3COOC_2H_5$
Molecular mass: 88.1

CAS # 141-78-6
RTECS # AH5425000
ICSC # 0367
UN # 1173
EC # 607-022-00-5



TYPES OF HAZARD/ EXPOSURE	ACUTE HAZARDS/ SYMPTOMS	PREVENTION	FIRST AID/ FIRE FIGHTING
FIRE	Highly flammable.	NO open flames, NO sparks, and NO smoking.	AFFF, alcohol-resistant foam, powder, carbon dioxide.
EXPLOSION	Vapour/air mixtures are explosive.	Closed system, ventilation, explosion-proof electrical equipment and lighting. Use non-sparking handtools.	In case of fire: keep drums, etc., cool by spraying with water.
EXPOSURE		PREVENT GENERATION OF MISTS!	
• **INHALATION**	Cough. Dizziness. Drowsiness. Headache. Nausea. Sore throat. Unconsciousness. Weakness.	Ventilation, local exhaust, or breathing protection.	Fresh air, rest. Artificial respiration if indicated. Refer for medical attention.
• **SKIN**	Dry skin.	Protective gloves. Protective clothing.	Remove contaminated clothes. Rinse skin with plenty of water or shower. Refer for medical attention.
• **EYES**	Redness. Pain.	Safety goggles, or eye protection in combination with breathing protection.	First rinse with plenty of water for several minutes (remove contact lenses if easily possible), then take to a doctor.
• **INGESTION**		Do not eat, drink, or smoke during work.	Rinse mouth. Give plenty of water to drink.

SPILLAGE DISPOSAL	STORAGE	PACKAGING & LABELLING
Evacuate danger area! Collect leaking and spilled liquid in sealable containers as far as possible. Absorb remaining liquid in sand or inert absorbent and remove to safe place. Do NOT wash away into sewer (extra personal protection: complete protective clothing including self-contained breathing apparatus).	Fireproof. Separated from strong oxidants. Cool. Well closed.	F symbol R: 11 S: (2-)16-23-29-33 UN Hazard Class: 3 UN Packing Group: II

SEE IMPORTANT INFORMATION ON BACK

ICSC: 0367

Prepared in the context of cooperation between the International Programme on Chemical Safety & the Commission of the European Communities © IPCS CEC 1993 No modifications to the International version have been made except to add the OSHA PELs, NIOSH RELs and IDLH values.

International Chemical Safety Cards

ETHYL ACETATE

ICSC: 0367

IMPORTANT DATA

PHYSICAL STATE; APPEARANCE:
COLOURLESS LIQUID , WITH CHARACTERISTIC ODOUR.

PHYSICAL DANGERS:
The vapour is heavier than air and may travel along the ground; distant ignition possible.

CHEMICAL DANGERS:
Heating may cause violent combustion or explosion. The substance decomposes under influence of UV light, bases, acids. Reacts with strong oxidants, bases or acids. Attacks aluminium and plastics.

OCCUPATIONAL EXPOSURE LIMITS (OELs):
TLV: 400 ppm; 1440 mg/m^3 A4 (ACGIH 1997).
OSHA PEL: TWA 400 ppm (1400 mg/m^3)
NIOSH REL: TWA 400 ppm (1400 mg/m^3)
NIOSH IDLH: 2000 ppm LEL

ROUTES OF EXPOSURE:
The substance can be absorbed into the body by inhalation of its vapour.

INHALATION RISK:
A harmful contamination of the air can be reached rather quickly on evaporation of this substance at 20°C.

EFFECTS OF SHORT-TERM EXPOSURE:
The substance irritates the eyes and the respiratory tract. The substance may cause effects on the central nervous system. Exposure far above the OEL may result in death.

EFFECTS OF LONG-TERM OR REPEATED EXPOSURE:
The liquid defats the skin.

PHYSICAL PROPERTIES	Boiling point: 77°C Melting point: -84°C Relative density (water = 1): 0.9 Solubility in water: very good Vapour pressure, kPa at 20°C: 10	Relative vapour density (air = 1): 3.0 Flash point: -4°C c.c. Auto-ignition temperature: 427°C Explosive limits, vol% in air: 2.2-11.5 Octanol/water partition coefficient as log Pow: 0.73
ENVIRONMENTAL DATA		

N O T E S

Use of alcoholic beverages enhances the harmful effect. Acetidin, Vinegar naphtha are trade names.

Transport Emergency Card: TEC (R)-76
NFPA Code: H1; F3; R0;

ADDITIONAL INFORMATION

ICSC: 0367 **ETHYL ACETATE**

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Level 1

Chemical Name: Ethyl acetate

CAS Registry Number: 141-78-6

Click on red circle(s) to obtain data.

Risk Value	ATSDR	Health Canada	ITER	RIVM	U.S.EPA	WHO/IPCS
Noncancer Oral	●	●	●	●	●	●
Cancer Oral	●	●	●	●	●	●
Noncancer Inhalation	●	●	●	●	●	●
Cancer Inhalation	●	●	●	●	●	●

Glossary of ITER definitions

ITER Instructions

WHAT'S NEW | SUPPORT ITER | ITER HOME | RETURN

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CTC Concurrent Technologies Corporation

Toxicology Excellence for Risk Assessment

TERA

NTP CHEMICAL REPOSITORY (RADIAN CORPORATION, AUGUST 29, 1991)
ETHYL ACETATE

-IDENTIFIERS
 ===========

*CATALOG ID NUMBER: 001668

*CAS NUMBER: 141-78-6

*BASE CHEMICAL NAME: ETHYLACETATE

*PRIMARY NAME: ETHYL ACETATE

*CHEMICAL FORMULA: C4H8O2

*STRUCTURAL FORMULA: CH3COOCH2CH3

*WLN: 2OV1

*SYNONYMS:
  ACETIC ACID, ETHYL ESTER
  ACETIC ETHER
  ACETOXYETHANE
  ETHYL ACETIC ESTER
  ETHYL ETHANOATE
  VINEGAR NAPHTHA
  ACETIDIN
  RCRA WASTE NUMBER U112
  UN 1173

-PHYSICAL CHEMICAL DATA
 ======================

*PHYSICAL DESCRIPTION: LITERATURE: Clear, colorless, mobile liquid
REPOSITORY: Clear colorless liquid

*MOLECULAR WEIGHT: 88.11

*SPECIFIC GRAVITY: 0.9003 @ 20/4 C [016,047,071]

*DENSITY: 0.8945 g/mL [043,062]

*MP (DEG C): -83.6 C [016,043,047,071]

*BP (DEG C): 77 C [031,058,346,451]

*SOLUBILITIES:
WATER : 50-100 mg/mL @ 21 C (RAD)

DMSO : >=100 mg/mL @ 21 C (RAD)

95% ETHANOL : >=100 mg/mL @ 21 C (RAD)

METHANOL : Not available

ACETONE : >=100 mg/mL @ 21 C (RAD)

TOLUENE : Not available

OTHER SOLVENTS:
Alcohol: Soluble [016,031,062,295]
Benzene: Soluble [016,047]
Ether: Soluble [031,205,295,421]
Chloroform: Soluble [031,205,295,421]
Most organic solvents: Miscible [029]

*VOLATILITY:
Vapor pressure: 73 mm Hg @ 20 C [058,062]; 100 mm Hg @ 27 C [038,043,051]
Vapor density : 3.04 [031,043,055,071]

*FLAMMABILITY(FLASH POINT):
This chemical has a flash point of -4 C (24 F) [043,295,371,451]. It is flammable. Fires involving this material can be controlled with a dry chemical, carbon dioxide or Halon extinguisher. The autoignition temperature is 426 C (800 F) [031,062,421,451].

*UEL: 11.5% [031,036,421,451] LEL: 2.0% [058,451]

*REACTIVITY:
This chemical may ignite or explode with lithium aluminum hydride [029,036,066,269]. It may also ignite with potassium tert-butoxide [036,043,066]. It is incompatible with nitrates, strong alkalies and strong acids [102,269,346]. It will attack some forms of plastics, rubber and coatings [102]. It is incompatible with oxidizers such as hydrogen peroxide, nitric acid, perchloric acid and chromium trioxide [058]. Violent reactions occur with chlorosulfonic acid [043,451].

*STABILITY:
This chemical is slowly hydrolyzed by moisture [029,031,269]. It is also sensitive to heat [058,071,102,269]. On prolonged storage, materials containing similar functional groups have formed explosive peroxides [058]. Solutions of this chemical in water, DMSO, 95% ethanol or acetone should be stable for 24 hours under normal lab conditions (RAD).

*OTHER PHYSICAL DATA:
Pleasant, fruity odor [071]
Odor threshold: 50 ppm [071,421]
Refractive index: 1.3723 @ 20 C [016,047]
log P octanol: 0.66-0.73 [055]
Critical temperature: 250 C [371]
Critical pressure: 38 atmospheres [371]
Liquid surface tension: 24 dynes/cm [371]
Evaporation rate (butyl acetate = 1): 4.5 [058]
Latent heat of vaporization: 87.6 cal/g [371]
Heat of combustion: -5816 cal/g [371]
Specific gravity: 0.9019 @ 20/20 C [058]
100% Volatile by volume [058]
Floats on water [058]

-TOXICITY
========

*NIOSH REGISTRY NUMBER: AH5425000

*TOXICITY:

typ. dose	mode	specie	amount	units	other
LCLo	ihl	cat	61	gm/m3	
LCLo	ihl	gpg	77	mg/m3/1H	

TCLo	ihl	hmn	400	ppm
LC50	ihl	mus	45	gm/m3/2H
LC50	ihl	rat	1600	ppm/8H
LD50	ipr	mus	709	mg/kg
LD50	orl	gpg	5500	mg/kg
LD50	orl	mus	4100	mg/kg
LD50	orl	rat	5620	mg/kg
LD50	orl	rbt	4935	mg/kg
LD50	scu	cat	3000	mg/kg
LD50	scu	gpg	3000	mg/kg
LDLo	scu	rat	5000	mg/kg

*AQTX/TLM96: Not available

*SAX TOXICITY EVALUATION:
THR: Moderately irritating to the eyes, mucous membranes, gums and respiratory tract. Prolonged inhalation can cause renal or hepatic damage. Prolonged contact can cause conjunctival irritation and corneal clouding. Poison by inhalation. Moderately toxic by intraperitoneal route. Mildly toxic by ingestion. Mutagenic data.

*CARCINOGENICITY: Not available

*MUTATION DATA: See RTECS printout for data

*TERATOGENICITY: Not available

*STANDARDS, REGULATIONS & RECOMMENDATIONS:
OSHA: Federal Register (1/19/89) and 29 CFR 1910.1000 Subpart Z
Transitional Limit: PEL-TWA 400 ppm [015,327,545,610]
Final Limit: PEL-TWA 400 ppm [015,545,610]
ACGIH: TLV-TWA 400 ppm [015,415,421,610]
NIOSH Criteria Document: None
NFPA Hazard Rating: Health (H): 1
Flammability (F): 3
Reactivity (R): 0
H1: Materials only slightly hazardous to health (see NFPA for details).
F3: Materials which can be ignited under almost all normal temperature conditions (see NFPA for details).
R0: Materials which are normally stable even under fire exposure conditions and which are not reactive with water (see NFPA for details).

*OTHER TOXICITY DATA:
Skin and Eye Irritation Data:
eye-hmn 400 ppm
Review: Toxicology Review
Standards and Regulations: DOT-Hazard: Flammable liquid; Label: Flammable liquid
Status: EPA Genetox Program 1988, Inconclusive: B subtilis rec assay
EPA TSCA Chemical Inventory, 1986
EPA TSCA Test Submission (TSCATS) Data Base, September 1989
IDLH value: 10000 ppm [058]

-OTHER DATA (Regulatory)
==========

*PROPER SHIPPING NAME (IATA): Ethyl acetate

*UN/ID NUMBER: UN1173

*HAZARD CLASS: 3 SUBSIDIARY RISK: None PACKING GROUP: II

*LABELS REQUIRED: Flammable liquid

*PACKAGING: PASSENGER: PKG. INSTR.: 305, Y305 MAXIMUM QUANTITY: 5 L, 1 L
CARGO : PKG. INSTR.: 307 MAXIMUM QUANTITY: 60 L

*SPECIAL PROVISIONS: None

*USES:
This compound is used in artificial fruit essences and as a solvent for varnishes, aeroplane dopes, coatings, plastics, lacquers, nitrocellulose, smokeless powders, organic synthesis and pharmaceuticals. It is used as an insect fumigant and in the manufacture of artificial leather, photographic film and plates, artificial silks, perfumes and cleaning textiles. It is also a synthetic flavoring substance and adjuvant.

*COMMENTS: Not available

-HANDLING PROCEDURES
==========

*ACUTE/CHRONIC HAZARDS:
This chemical is toxic by inhalation, ingestion or skin absorption [062,071,269]. It is an irritant of the skin, eyes, mucous membranes and respiratory tract. The vapor is heavier than air and can travel a considerable distance to a source of ignition and flash back [058]. When heated to decomposition it emits acrid smoke, irritating fumes and toxic fumes of carbon monoxide and carbon dioxide [043,058,269].

*MINIMUM PROTECTIVE CLOTHING: Not available

*RECOMMENDED GLOVE MATERIALS:
Permeation Test Results For The Neat (Undiluted) Chemical:
The permeation test results for the neat (undiluted) chemical are given below. The breakthrough times of this chemical are given for each glove type tested. The table is a presentation of actual test results, not specific recommendations or suggestions. Avoid glove types which exhibit breakthrough times of less than the anticipated task time plus an adequate safety factor. If this chemical makes direct contact with your glove, or if a tear, puncture or hole develops, replace them at once.

Glove Type	Model Number	Thickness	Breakthrough Time
Butyl rubber	North B-174	0.64 mm	420 min
Nitrile	North LA-142G	0.36 mm	8 min

*RECOMMENDED RESPIRATOR:
When working with this chemical, wear a NIOSH-approved full face chemical cartride respirator equipped with the appropriate organic vapor cartridges. If that is not available, a half face respirator similarly equipped plus airtight goggles can be substituted. However, please note that half face respirators provide a substantially lower level of protection than do full face respirators.

*OTHER: Not available

*STORAGE PRECAUTIONS:
You should keep this material in a tightly closed container under an inert atmosphere, and store it in an explosion-proof refrigerator. STORE AWAY FROM SOURCES OF IGNITION.

*SPILLS AND LEAKAGE:
If you spill this chemical, FIRST REMOVE ALL SOURCES OF IGNITION. Then, use absorbent paper to pick up all liquid spill material. Seal the absorbent paper, as well as any of your clothing which may be contaminated, in a vapor-tight plastic bag for eventual disposal. Wash any surfaces you may have contaminated with a soap and water solution. Do not reenter the contaminated area until the Safety Officer (or other responsible person) has verified that the area has been properly cleaned.

*DISPOSAL AND WASTE TREATMENT: Not available

-EMERGENCY PROCEDURES
==========

*SKIN CONTACT:
IMMEDIATELY flood affected skin with water while removing and isolating all contaminated clothing. Gently wash all affected skin areas thoroughly with soap and water.
If symptoms such as redness or irritation develop, IMMEDIATELY call a physician and be prepared to transport the victim to a hospital for treatment.

*INHALATION:
IMMEDIATELY leave the contaminated area; take deep breaths of fresh air. If symptoms (such as wheezing, coughing, shortness of breath, or burning in the mouth, throat, or chest) develop, call a physician and be prepared to transport the victim to a hospital.
Provide proper respiratory protection to rescuers entering an unknown atmosphere. Whenever possible, Self-Contained Breathing Apparatus (SCBA) should be used; if not available, use a level of protection greater than or equal to that advised under Respirator Recommendation.

*EYE CONTACT:
First check the victim for contact lenses and remove if present. Flush victim's eyes with water or normal saline solution for 20 to 30 minutes while simultaneously calling a hospital or poison control center.
Do not put any ointments, oils, or medication in the victim's eyes without specific instructions from a physician.
IMMEDIATELY transport the victim after flushing eyes to a hospital even if no symptoms (such as redness or irritation) develop.

*INGESTION:
DO NOT INDUCE VOMITING. Volatile chemicals have a high risk of being aspirated into the victim's lungs during vomiting which increases the medical problems.
If the victim is conscious and not convulsing, give 1 or 2 glasses of water to dilute the chemical and IMMEDIATELY call a hospital or poison control center. IMMEDIATELY transport the victim to a hospital.
If the victim is convulsing or unconscious, do not give anything by mouth, ensure that the victim's airway is open and lay the victim on his/her side with the head lower than the body. DO NOT INDUCE VOMITING. IMMEDIATELY transport the victim to a hospital.

*SYMPTOMS:
Symptoms of exposure to this compound include irritation of the eyes, mucous membranes, gums and respiratory tract [043,071]. Irritation of the nasal passages and throat may occur [058]. Skin irritation may also occur [062,269]. Prolonged contact may cause corneal clouding. Prolonged inhalation can cause renal or hepatic damage [043]. Prolonged inhalation may also cause damage to the lungs and heart [099]. Other symptoms include gastrointestinal

disturbances, nausea, headache and vomiting [269]. Exposure may cause narcosis and dermatitis [346]. It may also cause drowsiness, unconsciousness and sleepiness. High concentrations can cause stupor. Repeated or prolonged contact can cause drying of the skin and cracking [058]. Central nervous system depression may occur [295]. Chronic exposure may lead to anemia, leucocytosis, cloudy swelling and fatty degeneration of the viscera [043,071].

-SOURCES
=======

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New Jersey Department of Health and Senior Services

HAZARDOUS SUBSTANCE FACT SHEET

Common Name: **ETHYL ACETATE**

CAS Number: 141-78-6
DOT Number: UN 1173

RTK Substance number: 0841
Date: January 1986 Revision: June 1996

HAZARD SUMMARY

* **Ethyl Acetate** can affect you when breathed in and by passing through your skin.
* Exposure to high levels can cause you to feel dizzy, lightheaded, and to pass out.
* Repeated contact can cause drying and cracking of the skin.
* **Ethyl Acetate** can irritate the skin, eyes, nose and throat.
* **Ethyl Acetate** is a FLAMMABLE LIQUID and a FIRE HAZARD.

IDENTIFICATION

Ethyl Acetate is a colorless liquid with a fragrant, fruity odor. It is used as a solvent, a synthetic flavoring substance, and in making perfumes and dyes.

REASON FOR CITATION

* **Ethyl Acetate** is on the Hazardous Substance List because it is regulated by OSHA and cited by ACGIH, NFPA, NIOSH, DOT, HHAG and EPA.
* This chemical is on the Special Health Hazard Substance List because it is **FLAMMABLE.**
* Definitions are provided on page 5.

HOW TO DETERMINE IF YOU ARE BEING EXPOSED

The New Jersey Right to Know Act requires most employers to label chemicals in the workplace and requires public employers to provide their employees with information and training concerning chemical hazards and controls. The federal OSHA Hazard Communication Standard, 1910.1200, requires private employers to provide similar training and information to their employees.

* Exposure to hazardous substances should be routinely evaluated. This may include collecting air samples. Under OSHA 1910.20, you have a legal right to obtain copies of sampling results from your employer.
* If you think you are experiencing any work-related health problems, see a doctor trained to recognize occupational diseases. Take this Fact Sheet with you.

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* **ODOR THRESHOLD = 3.9 ppm**.
* The range of accepted odor threshold values is quite broad. Caution should be used in relying on odor alone as a warning of potentially hazardous exposures.

WORKPLACE EXPOSURE LIMITS

OSHA: The legal airborne permissible exposure limit (PEL) is **400 ppm** averaged over an 8-hour workshift.

NIOSH: The recommended airborne exposure limit is **400 ppm** averaged over a 10-hour workshift.

ACGIH: The recommended airborne exposure limit is **400 ppm** averaged over an 8-hour workshift.

* The above exposure limits are for air levels only. When skin contact also occurs, you may be overexposed, even though air levels are less than the limits listed above.

WAYS OF REDUCING EXPOSURE

* Where possible, enclose operations and use local exhaust ventilation at the site of chemical release. If local exhaust ventilation or enclosure is not used, respirators should be worn.
* Wear protective work clothing.
* Wash thoroughly immediately after exposure to **Ethyl Acetate** and at the end of the workshift.
* Post hazard and warning information in the work area. In addition, as part of an ongoing education and training effort, communicate all information on the health and safety hazards of **Ethyl Acetate** to potentially exposed workers.

This Fact Sheet is a summary source of information of all potential and most severe health hazards that may result from exposure. Duration of exposure, concentration of the substance and other factors will affect your susceptibility to any of the potential effects described below.

HEALTH HAZARD INFORMATION

Acute Health Effects

The following acute (short-term) health effects may occur immediately or shortly after exposure to **Ethyl Acetate**:

* **Ethyl Acetate** can irritate the skin, eyes, nose and throat.
* Exposure to high levels can cause you to feel dizzy, lightheaded, and to pass out.

Chronic Health Effects

The following chronic (long-term) health effects can occur at some time after exposure to **Ethyl Acetate** and can last for months or years:

Cancer Hazard

* According to the information presently available to the New Jersey Department of Health and Senior Services, **Ethyl Acetate** has been tested and has not been shown to cause cancer in animals.

Reproductive Hazard

* **Ethyl Acetate** may decrease fertility in males.

Other Long-Term Effects

* Repeated contact can cause drying and cracking of the skin.
* This chemical has not been adequately evaluated to determine whether brain or other nerve damage could occur with repeated exposure. However, many solvents and other petroleum-based chemicals have been shown to cause such damage. Effects may include reduced memory and concentration, personality changes (withdrawal, irritability), fatigue, sleep disturbances, reduced coordination, and/or effects on nerves supplying internal organs (autonomic nerves) and/or nerves to the arms and legs (weakness, "pins and needles").

MEDICAL

Medical Testing

Before beginning employment and at regular times after that, for those with frequent or potentially high exposures, the following is recommended:

* Evaluate for brain effects such as changes in memory, concentration, sleeping patterns and mood (especially irritability and social withdrawal), as well as headaches and fatigue. Consider evaluations of the cerebellar, autonomic and peripheral nervous systems. Positive and borderline individuals should be referred for neuropsychological testing.

Any evaluation should include a careful history of past and present symptoms with an exam. Medical tests that look for damage already done are not a substitute for controlling exposure.

Request copies of your medical testing. You have a legal right to this information under OSHA 1910.20.

WORKPLACE CONTROLS AND PRACTICES

Unless a less toxic chemical can be substituted for a hazardous substance, **ENGINEERING CONTROLS** are the most effective way of reducing exposure. The best protection is to enclose operations and/or provide local exhaust ventilation at the site of chemical release. Isolating operations can also reduce exposure. Using respirators or protective equipment is less effective than the controls mentioned above, but is sometimes necessary.

In evaluating the controls present in your workplace, consider: (1) how hazardous the substance is, (2) how much of the substance is released into the workplace and (3) whether harmful skin or eye contact could occur. Special controls should be in place for highly toxic chemicals or when significant skin, eye, or breathing exposures are possible.

In addition, the following controls are recommended:

* Where possible, automatically pump liquid **Ethyl Acetate** from drums or other storage containers to process containers.
* Before entering a confined space where **Ethyl Acetate** may be present, check to make sure that an explosive concentration does not exist.

Good **WORK PRACTICES** can help to reduce hazardous exposures. The following work practices are recommended:

* Workers whose clothing has been contaminated by **Ethyl Acetate** should change into clean clothing promptly.
* Contaminated work clothes should be laundered by individuals who have been informed of the hazards of exposure to **Ethyl Acetate**.
* On skin contact with **Ethyl Acetate**, immediately wash or shower to remove the chemical. At the end of the workshift, wash any areas of the body that may have contacted **Ethyl Acetate**, whether or not known skin contact has occurred.

* Do not eat, smoke, or drink where **Ethyl Acetate** is handled, processed, or stored, since the chemical can be swallowed. Wash hands carefully before eating or smoking.

PERSONAL PROTECTIVE EQUIPMENT

WORKPLACE CONTROLS ARE BETTER THAN PERSONAL PROTECTIVE EQUIPMENT. However, for some jobs (such as outside work, confined space entry, jobs done only once in a while, or jobs done while workplace controls are being installed), personal protective equipment may be appropriate.

The following recommendations are only guidelines and may not apply to every situation.

Clothing

* Avoid skin contact with **Ethyl Acetate**. Wear solvent-resistant gloves and clothing. Safety equipment suppliers/manufacturers can provide recommendations on the most protective glove/clothing material for your operation.
* All protective clothing (suits, gloves, footwear, headgear) should be clean, available each day, and put on before work.

Eye Protection

* Wear splash-proof chemical goggles when working with liquid, unless full facepiece respiratory protection is worn.

Respiratory Protection

IMPROPER USE OF RESPIRATORS IS DANGEROUS. Such equipment should only be used if the employer has a written program that takes into account workplace conditions, requirements for worker training, respirator fit testing and medical exams, as described in OSHA 1910.134.

* Where the potential exists for exposures over **400 ppm**, use a MSHA/NIOSH approved full facepiece respirator with an organic vapor cartridge/canister. Increased protection is obtained from full facepiece powered-air purifying respirators.
* If while wearing a filter, cartridge or canister respirator, you can smell, taste, or otherwise detect **Ethyl Acetate**, or in the case of a full facepiece respirator you experience eye irritation, leave the area immediately. Check to make sure the respirator-to-face seal is still good. If it is, replace the filter, cartridge, or canister. If the seal is no longer good, you may need a new respirator.
* Be sure to consider all potential exposures in your workplace. You may need a combination of filters, prefilters, cartridges, or canisters to protect against different forms of a chemical (such as vapor and mist) or against a mixture of chemicals.
* Where the potential for higher exposures exists, use a MSHA/NIOSH approved supplied-air respirator with a full facepiece operated in the positive pressure mode or with a full facepiece, hood, or helmet in the continuous flow mode, or use a MSHA/NIOSH approved self-contained breathing apparatus with a full facepiece operated in pressure-demand or other positive pressure mode.
* Exposure to **2,000 ppm** is immediately dangerous to life and health. If the possibility of exposures above **2,000 ppm** exists, use a MSHA/NIOSH approved self-contained breathing apparatus with a full facepiece operated in continuous flow or other positive pressure mode.

HANDLING AND STORAGE

* Prior to working with **Ethyl Acetate** you should be trained on its proper handling and storage.
* **Ethyl Acetate** must be stored to avoid contact with STRONG OXIDIZERS (such as CHLORINE, BROMINE, CHLORINE DIOXIDE and NITRATES); BASES (such as SODIUM HYDROXIDE and POTASSIUM HYDROXIDE); and STRONG ACIDS (such as SULFURIC ACID, HYDROCHLORIC ACID and NITRIC ACID) since violent reactions occur.
* Store in tightly closed containers in a cool, well-ventilated area away from HEAT.
* Sources of ignition, such as smoking and open flames, are prohibited where **Ethyl Acetate** is used, handled, or stored in a manner that could create a potential fire or explosion hazard.
* Metal containers involving the transfer of **Ethyl Acetate** should be grounded and bonded. Drums must be equipped with self-closing valves, pressure vacuum bungs, and flame arresters.
* Use only non-sparking tools and equipment, especially when opening and closing containers of **Ethyl Acetate**.
* Store in containers that are properly labeled with health hazard information and safe handling procedures.
* Wherever **Ethyl Acetate** is used, handled, manufactured, or stored, use explosion-proof electrical equipment and fittings.

QUESTIONS AND ANSWERS

Q: If I have acute health effects, will I later get chronic health effects?

A: Not always. Most chronic (long-term) effects result from repeated exposures to a chemical.

Q: Can I get long-term effects without ever having short-term effects?

A: Yes, because long-term effects can occur from repeated exposures to a chemical at levels not high enough to make you immediately sick.

Q: What are my chances of getting sick when I have been exposed to chemicals?
A: The likelihood of becoming sick from chemicals is increased as the amount of exposure increases. This is determined by the length of time and the amount of material to which someone is exposed.

Q: When are higher exposures more likely?
A: Conditions which increase risk of exposure include physical and mechanical processes (heating, pouring, spraying, spills and evaporation from large surface areas such as open containers), and "confined space" exposures (working inside vats, reactors, boilers, small rooms, etc.).

Q: Is the risk of getting sick higher for workers than for community residents?
A: Yes. Exposures in the community, except possibly in cases of fires or spills, are usually much lower than those found in the workplace. However, people in the community may be exposed to contaminated water as well as to chemicals in the air over long periods. Because of this, and because of exposure of children or people who are already ill, community exposures may cause health problems.

Q: Can men as well as women be affected by chemicals that cause reproductive system damage?
A: Yes. Some chemicals reduce potency or fertility in both men and women. Some damage sperm and eggs, possibly leading to birth defects.

The following information is available from:

New Jersey Department of Health and
Senior Services
Occupational Disease and Injury Services
Trenton, NJ 08625-0360
(609) 984-1863

Industrial Hygiene Information

Industrial hygienists are available to answer your questions regarding the control of chemical exposures using exhaust ventilation, special work practices, good housekeeping, good hygiene practices, and personal protective equipment including respirators. In addition, they can help to interpret the results of industrial hygiene survey data.

Medical Evaluation

If you think you are becoming sick because of exposure to chemicals at your workplace, you may call a Department of Health and Senior Services physician who can help you find the services you need.

Public Presentations

Presentations and educational programs on occupational health or the Right to Know Act can be organized for labor unions, trade associations and other groups.

Right to Know Information Resources

The Right to Know Infoline (609) 984-2202 can answer questions about the identity and potential health effects of chemicals, list of educational materials in occupational health, references used to prepare the Fact Sheets, preparation of the Right to Know survey, education and training programs, labeling requirements, and general information regarding the Right to Know Act. Violations of the law should be reported to (609) 984-2202.

DEFINITIONS

ACGIH is the American Conference of Governmental Industrial Hygienists. It recommends upper limits (called TLVs) for exposure to workplace chemicals.

A **carcinogen** is a substance that causes cancer.

The **CAS number** is assigned by the Chemical Abstracts Service to identify a specific chemical.

A **combustible** substance is a solid, liquid or gas that will burn.

A **corrosive** substance is a gas, liquid or solid that causes irreversible damage to human tissue or containers.

DEP is the New Jersey Department of Environmental Protection.

DOT is the Department of Transportation, the federal agency that regulates the transportation of chemicals.

EPA is the Environmental Protection Agency, the federal agency responsible for regulating environmental hazards.

A **fetus** is an unborn human or animal.

A **flammable** substance is a solid, liquid, vapor or gas that will ignite easily and burn rapidly.

The **flash point** is the temperature at which a liquid or solid gives off vapor that can form a flammable mixture with air.

HHAG is the Human Health Assessment Group of the federal EPA.

IARC is the International Agency for Research on Cancer, a scientific group that classifies chemicals according to their cancer-causing potential.

A **miscible** substance is a liquid or gas that will evenly dissolve in another.

mg/m^3 means milligrams of a chemical in a cubic meter of air. It is a measure of concentration (weight/volume).

MSHA is the Mine Safety and Health Administration, the federal agency that regulates mining. It also evaluates and approves respirators.

A **mutagen** is a substance that causes mutations. A **mutation** is a change in the genetic material in a body cell. Mutations can lead to birth defects, miscarriages, or cancer.

NAERG is the North American Emergency Response Guidebook. It was jointly developed by Transport Canada, the United States Department of Transportation and the Secretariat of Communications and Transportation of Mexico. It is a guide for first responders to quickly identify the specific or generic hazards of material involved in a transportation incident, and to protect themselves and the general public during the initial response phase of the incident.

NCI is the National Cancer Institute, a federal agency that determines the cancer-causing potential of chemicals.

NFPA is the National Fire Protection Association. It classifies substances according to their fire and explosion hazard.

NIOSH is the National Institute for Occupational Safety and Health. It tests equipment, evaluates and approves respirators, conducts studies of workplace hazards, and proposes standards to OSHA.

NTP is the National Toxicology Program which tests chemicals and reviews evidence for cancer.

OSHA is the Occupational Safety and Health Administration, which adopts and enforces health and safety standards.

PEOSHA is the Public Employees Occupational Safety and Health Act, a state law which sets PELs for New Jersey public employees.

ppm means parts of a substance per million parts of air. It is a measure of concentration by volume in air.

A **reactive** substance is a solid, liquid or gas that releases energy under certain conditions.

A **teratogen** is a substance that causes birth defects by damaging the fetus.

TLV is the Threshold Limit Value, the workplace exposure limit recommended by ACGIH.

The **vapor pressure** is a measure of how readily a liquid or a solid mixes with air at its surface. A higher vapor pressure indicates a higher concentration of the substance in air and therefore increases the likelihood of breathing it in.

>>>>>>>>>>>>>>>>> EMERGENCY INFORMATION <<<<<<<<<<<<<<<<<

Common Name: **ETHYL ACETATE**
DOT Number: **UN 1173**
NAERG Code: **129**
CAS Number: **141-78-6**

Hazard rating	NJDHSS	NFPA
FLAMMABILITY	-	3
REACTIVITY	-	0
POISONOUS GASES ARE PRODUCED IN FIRE CONTAINERS MAY EXPLODE IN FIRE		

Hazard Rating Key: 0=minimal; 1=slight; 2=moderate; 3=serious; 4=severe

FIRE HAZARDS

* **Ethyl Acetate** is a FLAMMABLE LIQUID.
* Use dry chemical, CO_2, or alcohol foam extinguishers. Water can be used to keep fire-exposed containers cool.
* POISONOUS GASES ARE PRODUCED IN FIRE.
* CONTAINERS MAY EXPLODE IN FIRE.
* Vapors may travel to a source of ignition and flash back.
* The vapor is heavier than air and may travel a distance to cause a fire or explosion far from the source.
* If employees are expected to fight fires, they must be trained and equipped as stated in OSHA 1910.156.

SPILLS AND EMERGENCIES

If **Ethyl Acetate** is spilled or leaked, take the following steps:

* Restrict persons not wearing protective equipment from area of spill or leak until clean-up is complete.
* Remove all ignition sources.
* Ventilate area of spill or leak.
* Absorb liquids in vermiculite, dry sand, earth, or a similar material and deposit in sealed containers.
* Keep **Ethyl Acetate** out of a confined space, such as a sewer, because of the possibility of an explosion, unless the sewer is designed to prevent the build-up of explosive concentrations.
* It may be necessary to contain and dispose of **Ethyl Acetate** as a HAZARDOUS WASTE. Contact your state Department of Environmental Protection (DEP) or your regional office of the federal Environmental Protection Agency (EPA) for specific recommendations.
* If employees are required to clean-up spills, they must be properly trained and equipped. OSHA 1910.120(q) may be applicable.

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FOR LARGE SPILLS AND FIRES immediately call your fire department. You can request emergency information from the following:

CHEMTREC: (800) 424-9300
NJDEP HOTLINE: (609) 292-7172

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HANDLING AND STORAGE (See page 3)

FIRST AID

In NJ, POISON INFORMATION 1-800-962-1253

Eye Contact

* Immediately flush with large amounts of water for at least 15 minutes, occasionally lifting upper and lower lids.

Skin Contact

* Remove contaminated clothing. Wash contaminated skin with soap and water.

Breathing

* Remove the person from exposure.
* Begin rescue breathing if breathing has stopped and CPR if heart action has stopped.
* Transfer promptly to a medical facility.

PHYSICAL DATA

Vapor Pressure: 76 mm Hg at 68^{o}F (20^{o}C)
Flash Point: 24^{o}F (-4.4^{o}C)
Water Solubility: Soluble

OTHER COMMONLY USED NAMES

Chemical Name:

Acetic Acid Ethyl Ester

Other Names:

Acetic Ether; Ethyl Acetic Ester; Ethyl Ethanoate; Acetic Ester

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Not intended to be copied and sold for commercial purposes.

NEW JERSEY DEPARTMENT OF HEALTH AND
SENIOR SERVICES
Right to Know Program
PO Box 368, Trenton, NJ 08625-0368
(609) 984-2202

Web Sites

that offer searchable chemical databases, recommended by Scorecard

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If you want more detailed information about a chemical than Scorecard provides, there are several on-line and library resources Scorecard recommends for further research.

ON-LINE CHEMICAL DATABASES

CambridgeSoft Chemfinder
http://chemfinder.camsoft.com/

Search

Chemfinder gives basic physico-chemical data and molecular structures for chemicals, and provides links to international data sources addressing specific chemicals.

Hazardous Substances Data Bank
http://toxnet.nlm.nih.gov/

Search

HSDB focuses on the toxicology of potentially hazardous chemicals, and includes peer-reviewed information on human exposure, industrial hygiene, emergency handling procedures, environmental fate, and regulatory requirements.

University of Akron Hazardous Chemicals Database
http://ull.chemistry.uakron.edu/erd/

Search

The Hazardous Chemicals Database provides physical data on chemicals and links to Department of Transportation safety guides that are valuable for emergency response.

BIBLIOGRAPHIC RESOURCES ON CHEMICAL TOXICITY

Scorecard provides qualitative summaries of the health hazards posed by a chemical (e.g., it is a suspected neurotoxicant), but not direct access to supporting toxicological data. These scientific studies are abstracted in several toxicity databases, which are available in libraries, from commercial vendors, and sometimes on-line. The major toxicity databases include:

The Registry of Toxic Effects of Chemicals Substances (RTECS)
RTECS is a database of toxicological information compiled by the National Institute for Occupational Safety and Health. It contains summary information about the types of health effects chemicals can cause and the concentrations at which toxicity is known to occur. It is available from several commercial vendors at http://www.cdc.gov/niosh/rtecs.html, and can often be found at major public or university libraries.

TOXLINE
Free access to the National Library of Medicine's toxicology-specific database of abstracts, reference journal articles, and reports is available at http://www.medscape.com/misc/FormToxlineInfLive.html

MEDLINE

Free access to the National Library of Medicine's MEDLINE database of more than 9 million references to articles published in 3800 biomedical journals is available at http://www.nlm.nih.gov/databases/freemedl.html. Two Web-based products, PubMed and Internet Grateful Med, provide this access. Medline can also be accessed at http://www.medscape.com/misc/FormMedlineInfLive.html

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ENVIRONMENTAL DEFENSE

finding the ways that work

Where Has All the Power Gone?

Updated: Monday, April 2, 2001
11:30 AM EDT



Environmental Defense economic analyst Daniel Kirshner recently joined trustee Rev. Sally Bingham for a forum on the energy shortage in California. Bingham helped found Episcopal Power & Light, which teaches about the impact of global warming and ways to decrease carbon dioxide emissions.

Streaming Audio
"Where Has All the Power Gone?"
Energy Forum from San Francisco's Grace Cathedral

- About Episcopal Power & Light
- Epicopal Power & Light's Regeneration Project
- EP&L and the Energy Shortage

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Frequently Asked Questions

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METHYL ETHYL KETONE (78-93-3)

summary from the About the Chemicals section of Scorecard

- **Human Health Hazards**

  Recognized: --

Suspected:		Reference(s)
	Cardiovascular or Blood Toxicant	KLAA
	Developmental Toxicant	EPA-HEN EPA-SARA JANK
	Gastrointestinal or Liver Toxicant	OEHHA-99
	Kidney Toxicant	OEHHA-99
	Neurotoxicant	DAN EPA-HEN EPA-SARA
	Reproductive Toxicant	EPA-SARA
	Respiratory Toxicant	EPA-HEN OEHHA-AREL RTECS
	Skin or Sense Organ Toxicant	EPA-HEN OEHHA-AREL RTECS

- **Hazard Rankings**

  More hazardous than most chemicals in 2 out of 10 ranking systems.

- **Chemical Use Profile**

  This is a high volume chemical with production exceeding 1 million pounds annually in the U.S.
  Used in at least 13 industries.
  Used in consumer products, building materials or furnishings that contribute to indoor air pollution.

- **Profile of Environmental Release and Waste Generation**

  For a list of the geographic areas, facilities, or industrial sectors which report the largest releases or transfers of this chemical to the Toxics Release Inventory, select what you want:

  - Rank States
  - Rank Counties
  - Rank Zip Codes
  - Rank Facilities
  - Rank Industrial Sectors

- **Regulatory Coverage**

  On at least 5 federal regulatory lists.

- **Basic Testing to Identify Chemical Hazards**

  1 of 8 basic tests to identify chemical hazards has not been conducted on this chemical, or is not publicly available.

- **Information Needed for Safety Assessment**

  Lacks at least some of the national data required for safety assessment.
  Scorecard has risk assessment data for this chemical.

- **Links**

  Additional information about this chemical may be available elsewhere in Scorecard.

  Other web sites specific to this chemical:

  - Agency for Toxic Substances and Disease Registry ToxFAQ
  - CalEPA Air Resources Board Toxic Air Contaminant Summary
  - EPA Health Effects Notebook for Hazardous Air Pollutants
  - EPA Integrated Risk Information System Report
  - EPA Office of Pollution Prevention and Toxics Chemical Fact Sheet
  - EPA Office of Pollution Prevention and Toxics Chemical Fact Summary
  - Environmental Writer Chemical Backgrounder
  - IPCS International Chemical Safety Card
  - International Toxicity Estimates for Risk (ITER) from the Toxicology Excellence for Risk Assessment
  - National Toxicology Program Health and Safety Information Sheet
  - New Jersey Fact Sheet

  If none of these sources meet your needs, you can try searching some other chemical database Web sites.

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Cardiovascular or Blood Toxicity Definition

from the Health Effects section of Scorecard

Cardiovascular and blood toxicity is defined as adverse effects on the cardiovascular or hematopoietic systems that result from exposure to chemical substances. The cardiovascular system is composed of the heart and blood vessels; the hematopoietic system is composed of various blood cell types: erythrocytes (red blood cells), leukocytes (white blood cells), and platelets. Exposure to cardiovascular toxicants can contribute to a variety of diseases, including elevated blood pressure (hypertension), hardening of the arteries (arteriosclerosis), abnormal heartbeat (cardiac arrhythmia),and decreased blood flow to the heart (coronary ischemia). Exposure to hematopoietic toxicants can reduce the oxygen carrying capacity of red blood cells, disrupt important immunological processes carried out by white blood cells, and induce cancer.

Because the cardiovascular system is complex, adverse effects resulting from exposure to chemicals can arise through a variety of mechanisms. Toxicants can contribute to cardiovascular disease by directly damaging cardiac and blood vessel tissue, initiating arteriosclerotic plaque formation, stimulating the inflammatory response, or causing kidney-related hypertension. Lead, carbon disulfide, arsenic, cadmium, ozone, and vinyl chloride have been implicated in the etiology of cardiovascular disease. These chemicals may produce functional changes, such as cardiac arrhythmias, that can have serious and often lethal consequences. They can also induce hypertension, a major cause of cardiac hypertrophy and heart failure. Several toxicants have been found to aggravate preexisting cardiovascular disease. Carbon disulfide and arsenic can irreversibly accelerate coronary heart disease.

The blood cells of the hematopoietic system can also be severely affected by chemical substances. For example, benzene, a component of motor fuel, is a hematopoietic toxin. Chronic exposure to benzene vapors leads to the decreased production of all types of blood cells (pancytopenia). The long-term effect of exposure to benzene is leukemia, a cancerous proliferation of white blood cells.

For further general information on chemicals and cardiovascular and blood toxicity, see the following references:

Balazs, T., J. Hanig, and E. Herman. Toxic Responses of the Cardiovascular System. Chapter 14 in Casarett and Doull's Toxicology, edited by C. Klaassen, M. Amdur, and J. Doull. New York: Pergamon Press, 1996.

Baskin, S. I. Principles of Cardiac Toxicology. Boca Raton, Fla.: CRC Press, 1991.

Smith, R. Toxic Responses of the Blood. Chapter 8 in Casarett and Doull's Toxicology, edited by C. Klaassen, M. Amdur, and J. Doull. New York: Pergamon Press, 1996.

Taylor, A. E. Cardiovascular Effects of Environmental Chemicals. Otolaryngology, Head and Neck Surgery. 114(2): 209-211. 1996.

Wilcosky, T. C. Solvent Exposure and Cardiovascular Disease. American Journal of Industrial Medicine. 19:569-586 1991.

More

- references used to compile the list of cardiovascular or blood toxicants
- list of cardiovascular or blood toxicants

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Cardiovascular or Blood Toxicity References

from the Health Effects section of Scorecard

There is no generally accepted source for an authoritative list of chemicals that are recognized to cause cardiovascular or blood toxicity.

EDF's list of suspect cardiovascular and blood toxicants is compiled from the following sources:

AEGL: US EPA, National Advisory Committee for Acute Exposure Guideline Levels for Hazardous Substances. Notices. 62 Federal Register: 58839-58851 (October 30, 1997)

BENO: Benowitz, N.L. Cardiotoxicity in the Workplace. Occupational Medicine. 7(3): 465- 477. 1992. (Table 1: Chemical Toxins and Cardiovascular Disease).

CAA-AQC: US Environmental Protection Agency, Office of Research and Development. Air Quality Criteria for Ozone and Related Photochemical Oxidants, Volume III Washington, DC. July 1996.
US Environmental Protection Agency, Office of Research and Development. Air Quality Criteria for Oxides of Nitrogen, Volume III Washington, DC. August 1993.
US Environmental Protection Agency, Office of Research and Development. Air Quality Criteria for Particulate Matter, Volume III Washington, DC. April 1996.
US Environmental Protection Agency, Office of Research and Development. Air Quality Criteria for Carbon Monoxide. Washington, DC, December 1991.

CAPCOA: California Environmental Protection Agency and California Air Pollution Control Officers Association. Air Toxics Hotspots Program Risk Assessment Guidance: Revised 1992 Risk Assessment Guidance and Draft Evaluation of Acute Non-Cancer Health Effects. Office of Environmental Health Hazard Assessment, CalEPA, Berkeley, CA. December 1994 and January 1995.

CARB-TAC: California Air Resources Board. Toxic Air Contaminant Identification List Summaries and Proposed Update to the Toxic Air Contaminant List. Air Resources Board, CalEPA, Sacramento, CA. January 1996 and December 1998. http://www.arb.ca.gov/toxics/tac/tac.htm.

EDF: See EDF's Custom Hazard Identification documentation.

EPA-HEN: US Environmental Protection Agency. Health Effects Notebook for Hazardous Air Pollutants. Review Draft. December 1994. http://www. epa.gov/ttn/uatw/hapindex.html

EPA-TRI: US Environmental Protection Agency. Addition of Certain Chemicals; Toxic Chemical Release Reporting; Community Right to Know. Proposed and Final Rules. 59 Federal Register 1788 (Jan 12, 1994); 59 Federal Register 61432 (November 30, 1994).

HEAST: EPA, Office of Research and Development. Health Effects Assessment Summary Tables. Electronic Handbook of Risk Assessment Values 9(6):6/30/00. Electronic Handbook Publishers, Redmond, WA. http://www.wolfenet.com/~sdwyer/ehrav.htm

KLAA: Klaassen, C., M. Amdur and J. Doull (eds.). Casarett and Doull's Toxicology. The Basic Science of Poisons, 5th Ed. Pergamon Press, NY. 1996. (Table 17-1: Cardiotoxicity of Key Pharmaceutical Agents, Table 17-2: Halogenated Hydrocarbons Reported to Have Arrhythmogenic Properties, Table

17-3: Cardiotoxicity of Selected Industrial Agents, Table 17-6: Vasculotoxic Agents: Heavy Metals, Table 17-7: Vasculotoxic Agents: Industrial and Environmental Agents, Table 17-8: Vasculotoxic Agents: Gases).

KRIS: Kristensen, T. S. Cardiovascular Diseases and the Work Environment. Scandinavian Journal of Work and Environmental Health. 15:245-264. 1989. (Table 5: Classification of possible risk factors for cardiovascular disease in the work environment).

LADO: LaDou, J. (ed.). Occupational Medicine. Appleton & Lange, Norwalk, CN. 1990. (Table 14-1: Chemicals associated with methemoglobinemia or oxidative hemolysis, Table 14-3: Toxic substances associated with acquired porphyria in humans, Table 14-4: Chemicals reported to cause aplastic anemia in an occupational setting, Table 14-5: Toxic agents associated with isolated thrombocytopenia, Table 19-1: Classification of cardiovascular diseases and possible toxic causes).

MALA: Malachowsky, M.J. Health Effects of Toxic Substances. Government Institutes. Rockville, MD. 1995. (Table 7-1: Chemicals affecting blood).

NJ-FS: New Jersey Department of Health Services. Right to Know Program, NJDOH, Trenton, NJ. http://www.state.nj.us/health/eoh/rtkweb/

OEHHA-2000: Office of Environmental Health Hazard Assessment, California Environmental Protection Agency. Air Toxics Hot Spots Program Risk Assessment Guidelines, Part III. February, 2000 (http://www.oehha.ca.gov/air/chronic_rels/22RELS2k.html) and May, 2000 (http://www.oehha.ca.gov/air/chronic_rels/42kChREL.html)

OEHHA-99: Office of Environmental Health Hazard Assessment, California Environmental Protection Agency. Air Toxics Hot Spots Program Risk Assessment Guidelines, Part III, Draft Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels. June 1999 (http://www.oehha.ca.gov/air/chronic_rels/RAGSII.html) and October, 1999 (http://www.oehha.ca.gov/air/chronic_rels/RAGSp3draft.html).

OEHHA-97: Office of Environmental Health Hazard Assessment, California Environmental Protection Agency. Draft Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels. October 1997. http://www.oehha.org/air/chronic_rels/GETRELS.html

OEHHA-AREL: Office of Environmental Health Hazard Assessment, California Environmental Protection Agency. All acute reference exposure levels developed by OEHHA as of May 2000. May, 2000. http://www.oehha.org/air/acute_rels/allAcRELs.html

RTECS: National Institute for Occupational Safety and Health's Registry of Toxic Effects of Chemical Substances. See EDF's Suspect Hazard Identification documentation.

STAC: Stacey, N.H. Occupational Toxicology. Taylor & Francis. 1995. (Table 3.16: Examples of haematopoietic injury from workplace exposure, Table 3.22: Workplace exposures implicated in cardiovascular disease).

More

- definition of cardiovascular or blood toxicity
- list of cardiovascular or blood toxicants

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Developmental Toxicity Definition

from the Health Effects section of Scorecard

Developmental toxicity is defined as adverse effects on the developing child that result from exposure to chemical substances. Sometimes called teratogens, developmental toxicants include agents that induce structural malformations and other birth defects, low birth weight, metabolic or biological dysfunction, and psychological or behavioral deficits that become manifest as the child grows. Developmental toxicity is often considered to be a subcategory of reproductive toxicity, but is treated as a distinct health endpoint in EDF's hazard identification system (see the separate definition of reproductive toxicity).

While developmental toxicity usually results from prenatal exposures to toxicants experienced by the mother, it can also result from paternal exposures, or from postnatal exposures experienced by a developing child. Maternal exposure to toxic chemicals during pregnancy can disrupt the development of or even cause the death of the fetus. Exposure of pregnant women to the developmental toxicant mercury, for example, has been shown to lower the birth weights of and cause severe brain damage in their children. Among the adverse effects associated with maternal exposure to toluene are central nervous system dysfunction, craniofacial and limb anomalies, and developmental delay. Dark brown pigmentation, shorter gestation time, and lower birth weight have been found in the children of women exposed to polychlorinated biphenyls (PCBs) during their pregnancies.

Paternal exposure to toxicants can cause male reproductive toxicity, such as sterility, and may contribute to early fetal loss or birth defects. For example, the occupational exposure of men to vinyl chloride has been associated with increased rates of spontaneous abortion in their wives. Early postnatal contact with toxicants (through contaminated food or air) can affect normal development. Exposure to secondhand tobacco smoke, for example, increases an infant’s risk of contracting respiratory infections or succumbing to sudden infant death syndrome.

For further general information on chemicals and developmental toxicity, see the following references:

Manson, J. Teratogens. Chapter 7 in Casarett and Doull's Toxicology, edited by C. Klaassen, M. Amdur, and J. Doull. New York: Pergamon Press, 1996.

Schardein, J. Chemically Induced Birth Defects. New York; Dekker, 1985.

More

- references used to compile the list of developmental toxicants
- list of developmental toxicants

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Developmental Toxicity References

from the Health Effects section of Scorecard

P65: The most current and authoritative list of chemicals that are recognized to cause developmental toxicity is California's Proposition 65 . Substances are placed on the Proposition 65 list of chemicals "known to the state of California to cause reproductive toxicity" if an independent science advisory board has concluded they possess sufficient evidence of such toxicity in animals or humans, or if an authoritative organization such as the National Toxicology Program have reached a similar conclusion, or if a federal regulatory agency requires a reproductive toxicity warning label. The Proposition 65 list identifies whether a chemical is a developmental toxicant. The current Proposition 65 List of Reproductive Toxicants (February 2001) can be obtained from http://www.oehha.ca.gov/prop65/prop65_list/Newlist.html.

A number of chemicals have toxicological evidence of developmental toxicity that currently does not satisfy the sufficiency criteria used to list agents under Proposition 65, or that has not yet been finally evaluated by hazard identification processes in the state of California or other authoritative agencies. EDF's list of suspect developmental toxicants is compiled from the following sources:

CAA-AQC: US Environmental Protection Agency, Office of Research and Development. Air Quality Criteria for Oxides of Nitrogen, Volume III Washington, DC. August 1993.
US Environmental Protection Agency, Office of Research and Development. Air Quality Criteria for Carbon Monoxide. Washington, DC, December 1991.

EDF: See EDF's Custom Hazard Identification documentation.>

EPA-HEN: US Environmental Protection Agency. Health Effects Notebook for Hazardous Air Pollutants. Review Draft. December 1994. http://www. epa.gov/ttn/uatw/hapindex.html

EPA-SARA: Roadmaps to Sources of Information on Chemicals Listed in the Emergency Planning Community and Community Right-to-Know Act (Also Known as SARA Title 3), Section 313 Toxic Release Inventory (for Microcomputers). (Report Number EPADFDK92040). 1991. Data file distributed in 2 diskettes by Office of Pollution, Prevention, and Toxics, Environmental Protection Agency, Washington, DC. NOTE: Datasource no longer being maintained by EPA; not currently available online.

EPA-TRI: US Environmental Protection Agency. Addition of Certain Chemicals; Toxic Chemical Release Reporting; Community Right to Know. Proposed and Final Rules. 59 Federal Register 1788 (Jan 12, 1994); 59 Federal Register 61432 (November 30, 1994).

JANK: Jankovic, J. A Screening Method for Occupational Reproductive Health Risk. American Industrial Hygiene Association Journal 57: 641-649. 1996.

NTP-R: Chapin, R.E. and R.A. Sloane. NIEHS/NTP Reproductive Assessment by Continuous Breeding: Evolving Study Design and Summaries of Ninety Studies. Environmental Health Perspectives 105, Supplement 1: 199-394. 1997.

OEHHA-2000: Office of Environmental Health Hazard Assessment, California Environmental Protection Agency. Air Toxics Hot Spots Program Risk Assessment Guidelines, Part III. February, 2000

(http://www.oehha.ca.gov/air/chronic_rels/22RELS2k.html) and May, 2000 (http://www.oehha.ca.gov/air/chronic_rels/42kChREL.html)

OEHHA-99: Office of Environmental Health Hazard Assessment, California Environmental Protection Agency. Air Toxics Hot Spots Program Risk Assessment Guidelines, Part III, Draft Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels. June 1999 (http://www.oehha.ca.gov/air/chronic_rels/RAGSII.html) and October, 1999 (http://www.oehha.ca.gov/air/chronic_rels/RAGSp3draft.html).

OEHHA-97: Office of Environmental Health Hazard Assessment, California Environmental Protection Agency. Draft Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels. October 1997. http://www.oehha.org/air/chronic_rels/GETRELS.html

P65-CAND: California EPA, Office of Environmental Health Hazard Assessment. Chemicals under consideration for listing via the authoritative bodies mechanisms. September 29, 2000. http://www.oehha.ca.gov/prop65/CRNR_notices/admin_listing/requests_info/callin19b.html
California EPA, Office of Environmental Health Hazard Assessment. Chemicals under consideration for listing via the authoritative bodies mechanisms. June 2, 2000. http://www.oehha.ca.gov/prop65/crnr_notices/admin_listing/requests_info/callin19a.html

P65-MC: Hazard identification based on an extension of a Proposition 65 listing. Substance is either a member of a class that is a recognized Propositon 65 hazard, or is a class that contains a member that is a recognized Propositon 65 hazard. See EDF's Member Class Hazard Identification documentation.

P65-PEND: California EPA, Office of Environmental Health Hazard Assessment. Notice of Intent to List Chemicals. February 23, 2001. http://oehha.ca.gov/prop65/CRNR_notices/admin_listing/intent_to_list/noilnimodipine.html
Office of Environmental Health Hazard Assessment. Notice of Intent to List Chemicals. December 29,2000. http://www.oehha.ca.gov/prop65/CRNR_notices/admin_listing/intent_to_list/noil19b1.html
California EPA, Office of Environmental Health Hazard Assessment. Notice of Intent to List Chemicals. August 25, 2000. http://www.oehha.ca.gov/prop65/CRNR_notices/admin_listing/intent_to_list/noil19a1.html
California EPA, Office of Environmental Health Hazard Assessment. Proposition 65 Notice of Intent to List Chemicals. October 29, 1999. http://www.oehha.org/prop65/CRNR_notices/admin_listing/intent_to_list/noilpk5B1.html
California EPA, Office of Environmental Health Hazard Assessment. Proposition 65 Notice of Intent to List Chemicals. April 23, 1999. http://www.oehha.org/prop65/CRNR_notices/admin_listing/intent_to_list/noil14a.html
California EPA, Office of Environmental Health Hazard Assessment. Proposition 65 Notice of Intent to List Chemicals. January 29,1999. http://www.oehha.org/prop65/CRNR_notices/admin_listing/intent_to_list/noil11a1.html
California EPA, Office of Environmental Health Hazard Assessment. Proposition 65 Notice of Intent to List Chemicals. December 5, 1997. http://www.oehha.org/prop65/CRNR_notices/admin_listing/intent_to_list/noil1297.html

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- list of developmental toxicants

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Gastrointestinal or Liver Toxicity Definitions

from the Health Effects section of Scorecard

Gastrointestinal and liver toxicity is defined as adverse effects on the structure and/or functioning of the gastrointestinal tract, liver, or gall bladder that result from exposure to chemical substances. The liver functions as a center for metabolism, processing chemicals we are exposed to so they can be utilized, detoxified, or excreted. While chemicals absorbed from the gastrointestinal tract are always processed by the liver, toxicants that enter the body through other routes of exposure can also reach the liver via its blood supply from the hepatic artery and the portal vein. The liver is frequently subject to injury induced by chemicals, called hepatotoxins, because of its role as the body's principal site of metabolism.

Necrosis, or liver cell death, is a common effect of acute exposure to hepatotoxic chemicals like beryllium, phosphorus, and urethane. The necrosis can be localized in specific areas of the liver or be more widespread. The liver is usually able to recover from necrosis because of its remarkable regenerative capacity. Exposure to hepatotoxic substances can also cause fatty liver (steatosis), hepatitis, jaundice, cholestasis, chronic liver damage (cirrhosis), and cancer. Carbon tetrachloride and related chemicals, such as chloroform, are linked to steatosis, necrosis, and cirrhosis of the liver. The most frequent cause of cirrhosis, however, is the habitual consumption of large quantities of alcohol. Cancer of the liver has been associated with occupational exposures to arsenic, copper, and vinyl chloride.

The gastrointestinal, or digestive, tract is composed of the esophagus, stomach, pancreas, and small and large intestines. The gastrointestinal tract is the site of entry for chemicals that are ingested. Exposure to chemicals that are toxic to the digestive tract can cause anorexia, nausea, vomiting, abdominal cramps, and diarrhea. There are four major types of tissue response to gastrointestinal injury from toxic agents: ulceration, necrosis, inflammation, and proliferation, including cancer. Some chemicals that cause gastrointestinal injury are halogenated aromatic hydrocarbons, including chlorobenzene and hexachlorobenzene, and such metals as lead, mercury, arsenic, and cadmium. Nitrosamines have been shown to cause colon cancer in humans.

For further general information on chemicals and gastrointestinal and liver toxicity, see the following references:

Britton, R. S. Metal-Induced Hepatotoxicity. Seminars in Liver Disease. 16(1): 3-12. 1996.

Plaa, G. Toxic Responses of the Liver. Chapter 10 in Casarett and Doull's Toxicology, edited by C. Klaassen, M. Amdur, and J. Doull. New York: Pergamon Press, 1996.

Rozman, K., ed. Gastrointestinal Toxicology. New York: Elsevier, 1986.

More

- references used to compile the list of gastrointestinal or liver toxicants
- list of gastrointestinal or liver toxicants

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Gastrointestinal or Liver Toxicity References

from the Health Effects section of Scorecard

There is no generally accepted source for an authoritative list of chemicals that are recognized to cause liver or gastrointestinal toxicity.

EDF's list of suspect liver or gastrointestinal toxicants is compiled from the following sources:

CAA-AQC: US Environmental Protection Agency, Office of Research and Development. Air Quality Criteria for Ozone and Related Photochemical Oxidants, Volume III Washington, DC. July 1996.

CAPCOA: California Environmental Protection Agency and California Air Pollution Control Officers Association. Air Toxics Hotspots Program Risk Assessment Guidance: Revised 1992 Risk Assessment Guidance and Draft Evaluation of Acute Non-Cancer Health Effects. Office of Environmental Health Hazard Assessment, CalEPA, Berkeley, CA. December 1994 and January 1995. http://www.oehha.org/air/hot_spots/index.html

CARB-TAC: California Air Resources Board. Toxic Air Contaminant Identification List Summaries and Proposed Update to the Toxic Air Contaminant List. Air Resources Board, CalEPA, Sacramento, CA. January 1996 and December 1998. http://www.arb.ca.gov/toxics/tac/tac.htm.

DIPA: DiPalma, J.A., J. Cunningham, J. Herrera, T. McCaffery, and D. Wolf. Occupational and Industrial Toxin Exposures and the Gastrointestinal Tract. American Journal of Gastroenterology. 86(9): 1107-1117. 1991. (Table 2: Selected Agents with Purported Digestive System Injury).

DOSS: Dossing, M. and P. Skinhoj. Occupational Liver Injury. Present State of Knowledge and Future Perspectives. International Archives of Occupational and Environmental Health. 56:1-21. 1985. (Table 2: Chemically induced liver injury: morphologic features and examples of confirmed and suspected causative agents).

EDF: See EDF's Custom Hazard Identification documentation.

EPA-HEN: US Environmental Protection Agency. Health Effects Notebook for Hazardous Air Pollutants. Review Draft. December 1994. http://www. epa.gov/ttn/uatw/hapindex.html

EPA-TRI: US Environmental Protection Agency. Addition of Certain Chemicals; Toxic Chemical Release Reporting; Community Right to Know. Proposed and Final Rules. 59 Federal Register 1788 (Jan 12, 1994); 59 Federal Register 61432 (November 30, 1994).

HEAST: EPA, Office of Research and Development. Health Effects Assessment Summary Tables. Electronic Handbook of Risk Assessment Values 9(6):6/30/00. Electronic Handbook Publishers, Redmond, WA. http://www.wolfenet.com/~sdwyer/ehrav.htm

KLAA: Klaassen, C., M. Amdur and J. Doull (eds.). Casarett and Doull's Toxicology. The Basic Science of Poisons, 5th Ed. Pergamon Press, NY. 1996. (Table 13-2: Types of Hepatic Injury).

LADO: LaDou, J. (ed.). Occupational Medicine. Appleton & Lange, Norwalk, CT. 1990. (Table 20-1: Chemical Agents associated with occupational liver disease, Table 20-4: Agents causing acute hepatic

injury).

MALA: Malachowsky, M.J. Health Effects of Toxic Substances. Government Institutes. Rockville, MD 1995. (Tables 7-2&3: Hepatotoxic Agents).

NJ-FS: New Jersey Department of Health Services. Right to Know Program, NJDOH, Trenton, NJ. http://www.state.nj.us/health/eoh/rtkweb/

OEHHA-97: Office of Environmental Health Hazard Assessment, California Environmental Protection Agency. Draft Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels. October 1997. http://www.oehha.org/air/chronic_rels/GETRELS.html

OEHHA-2000: Office of Environmental Health Hazard Assessment, California Environmental Protection Agency. Air Toxics Hot Spots Program Risk Assessment Guidelines, Part III. February, 2000 (http://www.oehha.ca.gov/air/chronic_rels/22RELS2k.html) and May, 2000 (http://www.oehha.ca.gov/air/chronic_rels/42kChREL.html)

OEHHA-99: Office of Environmental Health Hazard Assessment, California Environmental Protection Agency. Air Toxics Hot Spots Program Risk Assessment Guidelines, Part III, Draft Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels. June 1999 (http://www.oehha.ca.gov/air/chronic_rels/RAGSII.html) and October, 1999 (http://www.oehha.ca.gov/air/chronic_rels/RAGSp3draft.html).

OEHHA-97: Office of Environmental Health Hazard Assessment, California Environmental Protection Agency. Draft Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels. October 1997. http://www.oehha.org/air/chronic_rels/GETRELS.html

RTECS: National Institute for Occupational Safety and Health's Registry of Toxic Effects of Chemical Substances. See EDF's Suspect Hazard Identification documentation.

STAC: Stacey, N.H. Occupational Toxicology. Taylor & Francis. 1995. (Table 3.23: Clinical manifestations of chemical-induced gastrointestinal injury).

ZIMM: Zimmerman, H.J. and J.H. Lewis. Chemical- and Toxin- Induced Hepatotoxicity. Gastroenterology Clinics of North America. 24(4): 1027-1045. 1995. (Table 3: Forms of environmental hepatic injury).

More

- definition of gastrointestinal or liver toxicity
- list of gastrointestinal or liver toxicants

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Kidney Toxicity Definition

from the Health Effects section of Scorecard

Nephrotoxicity is defined as adverse effects on the kidney, ureter, or bladder that result from exposure to chemical substances. The kidney not only is the major excretory organ in the body, but also performs nonexcretory functions, such as regulating blood pressure and blood volume. Since the kidneys receive approximately 25 percent of cardiac output, any chemical in systemic circulation is delivered to them in relatively high amounts. This makes the kidney unusually susceptible to the toxic effects of chemicals. Some nephrotoxic agents cause acute injury to the kidney, while others produce chronic changes that can lead to end-stage renal failure or cancer. The consequences of renal failure can be profound, sometimes resulting in permanent damage that requires dialysis or kidney transplantation.

Toxic injury to the kidney is known to occur as a result of occupational, accidental, or therapeutic exposure to certain chemicals. Renal toxicants include halogenated hydrocarbons, such as carbon tetrachloride and trichloroethylene, and the heavy metals cadmium and lead.

For further general information on chemicals and kidney toxicity, see the following references:

Dixon, R. L., ed. Toxicology of the Kidney. Target Organ Toxicology Series. New York: Raven Press, 1981.

Hook, J., and W. Hewitt. Toxic Responses of the Kidney. Chapter 11 in Casarett and Doull's Toxicology, edited by C. Klaassen, M. Amdur, and J. Doull. New York: Pergamon Press, 1996.

International Programme on Chemical Safety (IPCS). Principles and Methods for the Assessment of Nephrotoxicity Associated with Exposure to Chemicals. Environmental Health Criteria, no. 119. Geneva: World Health Organization, 199l.

Landrigan, P.J., R. A. Goyer, T. W. Clarkson, D. P. Sandler, J. H. Smith, M. J. Thun, and R. Wedeen. The Work-Relatedness of Renal Disease. Archives of Environmental Health. 39(3): 225-230. 1984.

Wedeen, R. P. Renal Disease of Occupational Origin. Occupational Medicine. 7(3):449-461. 1992.

More

- references used to compile the list of kidney toxicants
- list of kidney toxicants

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Kidney Toxicity References

from the Health Effects section of Scorecard

There is no generally accepted source for an authoritative list of chemicals that are recognized to cause kidney toxicity.

EDF's list of suspect kidney toxicants is compiled from the following sources:

AEGL: US EPA, National Advisory Committee for Acute Exposure Guideline Levels for Hazardous Substances. Notices. 62 Federal Register: 58839-58851 (October 30, 1997).

CAPCOA: California Environmental Protection Agency and California Air Pollution Control Officers Association. Air Toxics Hotspots Program Risk Assessment Guidance: Revised 1992 Risk Assessment Guidance and Draft Evaluation of Acute Non-Cancer Health Effects. Office of Environmental Health Hazard Assessment, CalEPA, Berkeley, CA. December 1994 and January 1995. http://www.oehha.org/air/hot_spots/index.html

EDF: See EDF's Custom Hazard Identification documentation.

EPA-HEN: US Environmental Protection Agency. Health Effects Notebook for Hazardous Air Pollutants. Review Draft. December 1994. http://www. epa.gov/ttn/uatw/hapindex.html

EPA-TRI: US Environmental Protection Agency. Addition of Certain Chemicals; Toxic Chemical Release Reporting; Community Right to Know. Proposed and Final Rules. 59 Federal Register 1788 (Jan 12, 1994); 59 Federal Register 61432 (November 30, 1994).

KLAA: Klaassen, C., M. Amdur and J. Doull (eds.). Casarett and Doull's Toxicology. The Basic Science of Poisons, 5th Ed. Pergamon Press, NY. 1996. (Table 14-2: Examples of Nephrotoxic Therapeutic Agents, Table 14-3: Examples of Environmental Nephrotoxicants).

LAND: Landrigan, P.J., Goyer, R.A. Clarkson, T.W., Sandler, D.P., Smith, J.H., Thun, M.J., and R. Wedeen. The Work-Relatedness of Renal Disease. Archives of Environmental Health. 39(3): 225-230. 1984. (Table 2: Estimated Numbers of Workers in the United States with Potential Occupational Exposures to Known or Suspect Nephrotoxins).

NJ-FS: New Jersey Department of Health Services. Right to Know Program, NJDOH, Trenton, NJ. http://www.state.nj.us/health/eoh/rtkweb/

OEHHA-2000: Office of Environmental Health Hazard Assessment, California Environmental Protection Agency. Air Toxics Hot Spots Program Risk Assessment Guidelines, Part III. February, 2000 (http://www.oehha.ca.gov/air/chronic_rels/22RELS2k.html) and May, 2000 (http://www.oehha.ca.gov/air/chronic_rels/42kChREL.html)

OEHHA-99: Office of Environmental Health Hazard Assessment, California Environmental Protection Agency. Air Toxics Hot Spots Program Risk Assessment Guidelines, Part III, Draft Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels. June 1999 (http://www.oehha.ca.gov/air/chronic_rels/RAGSII.html) and October, 1999

(http://www.oehha.ca.gov/air/chronic_rels/RAGSp3draft.html).

OEHHA-97: Office of Environmental Health Hazard Assessment, California Environmental Protection Agency. Draft Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels. October 1997. http://www.oehha.org/air/chronic_rels/GETRELS.html

RTECS: National Institute for Occupational Safety and Health's Registry of Toxic Effects of Chemical Substances. See EDF's Suspect Hazard Identification documentation.

STAC: Stacey, N.H. Occupational Toxicology. Taylor & Francis. 1995. (Table 3.8: Examples of workplace exposures that have resulted in renal toxicity).

More

- definition of kidney toxicity
- list of kidney toxicants

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Reproductive Toxicity Definition

from the Health Effects section of Scorecard

Reproductive toxicity is defined as adverse effects on the male and female reproductive systems that result from exposure to chemical substances. Reproductive toxicity may be expressed as alterations in sexual behavior, decreases in fertility, or loss of the fetus during pregnancy. A reproductive toxicant may interfere with the sexual functioning or reproductive ability of exposed individuals from puberty throughout adulthood. Developmental toxicity (adverse effects on the developing child, such as birth defects) is often considered to be a subcategory of reproductive toxicity, but is treated as a distinct health endpoint in EDF's hazard identification system (see the separate definition of developmental toxicity).

Toxicants that target the female reproductive system can cause a wide variety of adverse effects. Changes in sexual behavior, onset of puberty, cyclicity, fertility, gestation time, pregnancy outcome, and lactation as well as premature menopause are among the potential manifestations of female reproductive toxicity: all can disrupt a woman’s ability to successfully reproduce. Exposure to lead, for example, can result in menstrual disorders and infertility. The toxicants carbon disulfide, mercury, and polychlorinated biphenyls (PBCs) have been shown to cause irregularities in the menstrual cycle. An increased rate of spontaneous abortion has been found in hospital workers exposed to ethylene oxide.

Toxicants that target the male reproductive system can affect sperm count or shape, alter sexual behavior, and/or increase infertility. Carbon disulfide and the pesticides chlordecone (kepone), ethylene dibromide (EDB), and dibromochloropropane (DBCP) are examples of chemicals known to disrupt male reproductive health. These toxicants have lowered the sperm counts of exposed individuals. Occupational exposure to DBCP has caused azoospermia (the total absence of sperm in the semen) and sterility.

For further general information on chemicals and reproductive toxicity, see the following references:

Dixon, R. Toxic Responses of the Reproductive System. Chapter 16 in Casarett and Doull's Toxicology, edited by C. Klaassen, M. Amdur, and J. Doull. New York: Pergamon Press, 1996.

US General Accounting Office. Reproductive and Developmental Toxicants, Regulatory Actions Provide Uncertain Protection (GAO/PEMD-92-3). Washington, D.C.: Government Printing Office, 1991.

More

- references used to compile the list of reproductive toxicants
- list of reproductive toxicants

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Reproductive Toxicity References

from the Health Effects section of Scorecard

P65: The most current and authoritative list of chemicals that are recognized to cause reproductive toxicity is California's Proposition 65 . Substances are placed on the Proposition 65 list of chemicals "known to the state of California to cause reproductive toxicity" if an independent science advisory board has concluded they possess sufficient evidence of such toxicity in animals or humans, or if an authoritative organization such as the National Toxicology Program have reached a similar conclusion, or if a federal regulatory agency requires a reproductive toxicity warning label. The Proposition 65 list identifies whether a chemical is a male or female reproductive toxicant. The current Proposition 65 List of Reproductive Toxicants (February 2001) can be obtained from http://www.oehha.ca.gov/prop65/prop65_list/Newlist.html.

A number of chemicals have toxicological evidence of reproductive toxicity that currently does not satisfy the sufficiency criteria used to list agents under Proposition 65, or that has not yet been finally evaluated by hazard identification processes in the state of California or other authoritative agencies. EDF's list of suspect reproductive toxicants is compiled from the following sources:

CAPCOA: California Environmental Protection Agency and California Air Pollution Control Officers Association. Air Toxics Hotspots Program Risk Assessment Guidance: Revised 1992 Risk Assessment Guidance and Draft Evaluation of Acute Non-Cancer Health Effects. Office of Environmental Health Hazard Assessment, CalEPA, Berkeley, CA. December 1994 and January 1995. http://www.oehha.org/air/acute_rels/acuterel.html

EDF: See EDF's Custom Hazard Identification documentation.

EPA-HEN: US Environmental Protection Agency. Health Effects Notebook for Hazardous Air Pollutants. Review Draft. December 1994. http://www. epa.gov/ttn/uatw/hapindex.html

EPA-SARA: Roadmaps to Sources of Information on Chemicals Listed in the Emergency Planning Community and Community Right-to-Know Act (Also Known as SARA Title 3), Section 313 Toxic Release Inventory (for Microcomputers). (Report Number EPADFDK92040). 1991. Data file distributed in 2 diskettes by Office of Pollution, Prevention, and Toxics, Environmental Protection Agency, Washington, DC. NOTE: Datasource no longer being maintained by EPA; not currently available online.

EPA-TRI: US Environmental Protection Agency. Addition of Certain Chemicals; Toxic Chemical Release Reporting; Community Right to Know. Proposed and Final Rules. 59 Federal Register 1788 (Jan 12, 1994); 59 Federal Register 61432 (November 30, 1994).

JANK: Jankovic, J. A Screening Method for Occupational Reproductive Health Risk. American Industrial Hygiene Association Journal. 57: 641-649. 1996.

KEMI-DAN: Hass U et al. Reproductive Toxicants in the Working Environment (In Danish.). Reproduktionsskadende kemiske stoffer i arbejdsmiljoet. AMI- rapport Nr. 35/1991. National Institute of Occupational Health, Copenhagen, DK. 1991.

NTP-R: Chapin, R.E. and R.A. Sloane. NIEHS/NTP Reproductive Assessment by Continuous Breeding:

Evolving Study Design and Summaries of Ninety Studies. Environmental Health Perspectives 105, Supplement 1: 199-394. 1997.

OEHHA-2000: Office of Environmental Health Hazard Assessment, California Environmental Protection Agency. Air Toxics Hot Spots Program Risk Assessment Guidelines, Part III. February, 2000 (http://www.oehha.ca.gov/air/chronic_rels/22RELS2k.html) and May, 2000 (http://www.oehha.ca.gov/air/chronic_rels/42kChREL.html)

OEHHA-99: Office of Environmental Health Hazard Assessment, California Environmental Protection Agency. Air Toxics Hot Spots Program Risk Assessment Guidelines, Part III, Draft Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels. June 1999 (http://www.oehha.ca.gov/air/chronic_rels/RAGSII.html) and October, 1999 (http://www.oehha.ca.gov/air/chronic_rels/RAGSp3draft.html).

OEHHA-97: Office of Environmental Health Hazard Assessment, California Environmental Protection Agency. Draft Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels. October 1997. http://www.oehha.org/air/chronic_rels/GETRELS.html

P65-CAND: California EPA, Office of Environmental Health Hazard Assessment. Chemicals under consideration for listing via the authoritative bodies mechanisms. September 29, 2000. http://www.oehha.ca.gov/prop65/CRNR_notices/admin_listing/requests_info/callin19b.html
California EPA, Office of Environmental Health Hazard Assessment. Chemicals under consideration for listing via the authoritative bodies mechanisms. June 2, 2000. http://www.oehha.ca.gov/prop65/crnr_notices/admin_listing/requests_info/callin19a.html

P65-MC: Hazard identification based on an extension of a Proposition 65 listing. Substance is either a member of a class that is a recognized Propositon 65 hazard, or is a class that contains a member that is a recognized Propositon 65 hazard. See EDF's Member Class Hazard Identification documentation.

P65-PEND: California EPA, Office of Environmental Health Hazard Assessment. Notice of Intent to List Chemicals. Decmebr 29,2000. http://www.oehha.ca.gov/prop65/CRNR_notices/admin_listing/intent_to_list/noil19b1.html
California EPA, Office of Environmental Health Hazard Assessment. Notice of Intent to List Chemicals. August 25, 2000. http://www.oehha.ca.gov/prop65/CRNR_notices/admin_listing/intent_to_list/noil19a1.html
California EPA, Office of Environmental Health Hazard Assessment. Proposition 65 Notice of Intent to List Chemicals. April 23, 1999. http://www.oehha.org/prop65/CRNR_notices/admin_listing/intent_to_list/noil14a.html
California EPA, Office of Environmental Health Hazard Assessment. Proposition 65 Notice of Intent to List Chemicals. March 19, 1999. http://www.oehha.org/prop65/CRNR_notices/admin_listing/intent_to_list/noilpkg1.html
California EPA, Office of Environmental Health Hazard Assessment. Proposition 65 Notice of Intent to List Chemicals. December 5, 1997. http://www.oehha.org/prop65/CRNR_notices/admin_listing/intent_to_list/noil1297.html

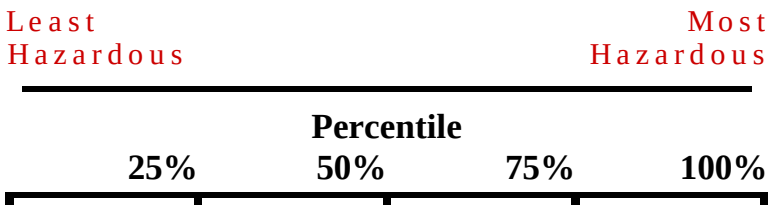
More

- definition of reproductive toxicity
- list of reproductive toxicants

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Hazard Rankings

for METHYL ETHYL KETONE (78-93-3) from Scorecard



Human Health Rankings

Toxicity only

- Ingestion Toxicity Weight (RSEI)
- Inhalation Toxicity Weight (RSEI)
- Human Health Effects Score (UTN)

Toxicity and exposure potential

- Noncancer Risk Score - Air Releases (EDF)
- Noncancer Risk Score - Water Releases (EDF)
- Worker Exposure Hazard Score (IRCH)

Ecological Health Rankings

Toxicity only

- Ecological Effects Score (UTN)

Toxicity and persistence

- Environmental Hazard Value Score (IRCH)

Integrated Environmental Rankings

Combined human and ecological scores

- Total Hazard Value Score (IRCH)
- Total Hazard Value Score (UTN)

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Industrial Uses

for METHYL ETHYL KETONE (78-93-3) from Scorecard

This is a high volume chemical with production exceeding 1 million pounds annually in the U.S.

Which Industries Use This Chemical?	**How is the Chemical Used in This Industry?**
Adhesives Manufacture	Carpet adhesive solvents
Electroplating	Electroplating - Cold-cleaning Solvents
Electroplating	Electroplating - Vapor Degreasing Solvents
Laboratory Chemicals	Solvents - Extraction
Machinery Mfg and Repair	Solvents - Machinery Manufacture and Repair
Metal Degreasing	Solvents - Metal Degreasing
Paint Manufacture	Solvents, Not Elsewhere Classified
Paint Stripping	Solvents - Paint Stripping
Paper Coating	Solvents
Pesticide Mfg (Insecticides)	Solvents - Insecticide Manufacture
Printing	Solvents for Flexography
Printing	Solvents for Gravure Printing
Reprographic Agents	Diazotype Materials - Misc. Chemicals
Rubber Manufacture	Solvents - Rubber Manufacture
Wood Stains and Varnishes	Varnish Solvents

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Consumer Products

that contain METHYL ETHYL KETONE (78-93-3) from Scorecard

What kinds of consumer products may contain this chemical?

- Acid nonhousehold metal cleaners (liquid)
- Aerosol paint concentrates
- Architectural coatings
- Auto, other transportation, and machinery refinish paints incl primers
- Automobile body polish and cleaners
- General performance sealants (PVAC, butyl, vinyl, etc.)
- Gravure inks
- Ground/traffic marking coatings
- Household hard surface cleaners (aerosol)
- Household hard surface cleaners (liquid)
- Household tints and dyes
- Industrial particleboard (furniture, fixtures, cabinets, etc.)
- Inks, writing and stamp pad inks (excl drawing and printing inks)
- Laundry starch preparations
- Lubricating oils
- Markers, fine point and broad tipped
- Misc. use aromatics
- Miscellaneous agricultural/pesticidal products
- Miscellaneous paint-related products
- Nail enamel and polish removers
- Nonstructural caulking compounds and sealants
- Other art materials incl clay, water & tempera colors, finger paint, etc.
- Other automotive chemicals
- Other industrial chemical specialty products
- Other manicuring preparations
- Other miscellaneous allied paint products, including brush cleaners
- Other specialty cleaning and sanitation products
- Paint and varnish removers
- Paint thinners
- Shoe polishes and cleaners
- Solvent thinned interior clear finishes
- Solvent thinned interior stains

- Solvent thinned interior undercoaters and primers
- Specialty performance sealants
- Surfactants, finishing agents, and assistants
- Synthetic resin and rubber adhesives
- Waterproofing compounds

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Scorecard's Source for Environmental Release and Waste Management Data

from Scorecard

Scorecard's source for information about chemical releases and waste management from manufacturing facilities is the U.S. Environmental Protection Agency's Toxics Release Inventory. The TRI database was established by Section 313 of the Emergency Planning and Community Right-To-Know Act of 1986 (EPCRA).

Under EPCRA, manufacturing facilities in specific industries are required to report their environmental releases and chemical waste management annually to EPA. Covered facilities must disclose their releases of approximately 650 toxic chemicals and chemical categories to air, water, and land, as well as the quantities of chemicals they recycle, treat, burn, or otherwise dispose of on-site and off-site. The specific categories of releases, transfers and overall waste generation reported to TRI are explained by Scorecard's Definitions of Toxics Release Inventory Reporting Categories.

Scorecard's 1998 TRI data is derived from the reports of 23,500 manufacturing and federal facilities. Seven "new" industries (e.g., mining and electric power generation) were required to report their release and waste management data for the first time in 1998, substantially increasing the total amount of chemicals tracked by TRI.

In 1998, facilities reported a total of 7.3 billion pounds of releases to air, land, water and underground injection. "Original" industries (required to report to TRI prior to 1997) reported approximately 2.4 billion pounds, or 32.6%, of the 7.3 billion pounds. Facilities in the new sectors reported almost 4.9 billion pounds, or 67.4%, of the 7.3 billion pounds. Reporting from the new industries accounted for 91.7 % of the land releases on-site, 38.8% of the air releases, 21.2 % of the releases to underground injection wells, and 3.5% of the discharges to surface water.

THE LIMITS OF TRI DATA

While TRI is the most comprehensive national source of information about toxic chemical releases, it has critical limitations:

1) TRI does not cover all toxic chemicals that have the potential to adversely affect human health or the environment.

2) TRI does not require reporting from many major sources of pollution releases.

3) TRI does not require companies to report the quantities of toxic chemicals used or the amounts that remain in products.

4) TRI does not provide information about the exposures people may experience as a consequence of chemical use.

WHAT NEW POLLUTION SOURCES ARE COVERED FOR THE FIRST TIME BY 1998 TRI DATA

Seven "new" industries only began reporting to TRI in 1998, and now dominate most rankings based on environmental releases:

Metal mining
Coal mining
Electric utilities
Commercial hazardous-waste treatment
Petroleum bulk terminals
Chemical wholesalers
Solvent recovery services

SCORECARD'S SOURCE FOR TRI DATA

All environmental release data in Scorecard are derived from the U.S. Environmental Protection Agency's public release of the 1998 TRI database. Issues related to the quality of 1998 TRI data used in Scorecard are explained in How Reliable Are TRI Data?

MORE ON TRI

Other websites related to TRI:

U.S. EPA Toxics Release Inventory: Community Right-to-Know Homepage http://www.epa.gov/tri/

U.S. EPA Envirofacts Warehouse Toxics Release Inventory: TRI Overview
http://www.epa.gov/enviro/html/tris/tris_overview.html

RTK Net: The Right-to-Know Network http://www.rtk.net/trisearch.html

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States with Reported Total Environmental Releases

of METHYL ETHYL KETONE (78-93-3) from the About The Chemicals section of Scorecard

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Ranked by (select your ranking criteria)

Total environmental releases Go (explain)

1. TEXAS: 5,236,767 Pounds
2. OHIO: 3,282,734 Pounds
3. INDIANA: 3,077,335 Pounds
4. MISSISSIPPI: 2,684,597 Pounds
5. PENNSYLVANIA: 2,462,291 Pounds
6. NORTH CAROLINA: 2,447,000 Pounds
7. ALABAMA: 2,350,138 Pounds
8. VIRGINIA: 2,083,585 Pounds
9. ILLINOIS: 1,713,396 Pounds
10. MICHIGAN: 1,457,248 Pounds
11. WISCONSIN: 1,441,837 Pounds
12. LOUISIANA: 1,440,410 Pounds
13. GEORGIA: 1,437,893 Pounds
14. SOUTH CAROLINA: 1,319,978 Pounds
15. TENNESSEE: 1,287,971 Pounds
16. MISSOURI: 1,186,766 Pounds
17. OREGON: 1,062,273 Pounds
18. WASHINGTON: 1,043,965 Pounds
19. MINNESOTA: 875,818 Pounds
20. WEST VIRGINIA: 856,675 Pounds
21. ARKANSAS: 759,052 Pounds
22. KANSAS: 746,333 Pounds
23. CALIFORNIA: 743,640 Pounds
24. KENTUCKY: 649,014 Pounds
25. NEW YORK: 639,203 Pounds
26. OKLAHOMA: 638,767 Pounds
27. FLORIDA: 507,772 Pounds
28. NEW JERSEY: 483,762 Pounds

29. MASSACHUSETTS: 473,695 Pounds
30. IOWA: 361,406 Pounds
31. RHODE ISLAND: 311,987 Pounds
32. CONNECTICUT: 267,972 Pounds
33. PUERTO RICO: 251,541 Pounds
34. IDAHO: 241,395 Pounds
35. MARYLAND: 224,678 Pounds
36. NEBRASKA: 220,653 Pounds
37. NEW HAMPSHIRE: 194,686 Pounds
38. ARIZONA: 191,467 Pounds
39. COLORADO: 146,255 Pounds
40. UTAH: 92,705 Pounds
41. DELAWARE: 51,303 Pounds
42. SOUTH DAKOTA: 43,069 Pounds
43. NORTH DAKOTA: 39,172 Pounds
44. VERMONT: 26,747 Pounds
45. MAINE: 17,852 Pounds
46. MONTANA: 15,477 Pounds
47. NEVADA: 14,704 Pounds
48. NEW MEXICO: 4,250 Pounds

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Counties with Reported Total Environmental Releases

of METHYL ETHYL KETONE (78-93-3) from the About The Chemicals section of Scorecard

---

Ranked by (select your ranking criteria)

Total environmental releases

in

Entire United States Go (explain)

1. JEFFERSON, TX: 1,782,555 pounds
2. LOWNDES, MS: 1,557,600 pounds
3. WICHITA, TX: 917,582 pounds
4. JACKSON, OR: 897,100 pounds
5. COOK, IL: 875,475 pounds
6. LUCAS, OH: 791,337 pounds
7. HARRIS, TX: 784,325 pounds
8. VENANGO, PA: 693,020 pounds
9. LAKE, IN: 667,643 pounds
10. SUMTER, GA: 608,225 pounds
11. HOUSTON, AL: 591,198 pounds
12. ALCORN, MS: 582,320 pounds
13. DANE, WI: 556,619 pounds
14. BEDFORD (CITY), VA: 500,000 pounds
15. GRANVILLE, NC: 473,200 pounds
16. CALCASIEU, LA: 424,339 pounds
17. CADDO, LA: 419,351 pounds
18. KING, WA: 393,938 pounds
19. SNOHOMISH, WA: 381,982 pounds
20. LAUDERDALE, TN: 380,000 pounds
21. MCKEAN, PA: 362,355 pounds
22. SEDGWICK, KS: 359,521 pounds
23. TRUMBULL, OH: 352,648 pounds
24. BRUNSWICK, NC: 351,000 pounds
25. COLBERT, AL: 350,251 pounds

26. PORTER, IN: 297,763 pounds
27. KENT, MI: 289,514 pounds
28. WINCHESTER (CITY), VA: 287,874 pounds
29. JEFFERSON, WV: 280,000 pounds
30. SPARTANBURG, SC: 267,918 pounds
31. TULSA, OK: 267,705 pounds
32. HENNEPIN, MN: 259,366 pounds
33. TUSCALOOSA, AL: 256,227 pounds
34. MARSHALL, IN: 254,907 pounds
35. CUYAHOGA, OH: 248,640 pounds
36. SCHUYLKILL, PA: 247,640 pounds
37. YABUCOA, PR: 241,000 pounds
38. EAST BATON ROUGE, LA: 240,986 pounds
39. HEMPSTEAD, AR: 238,756 pounds
40. DALLAS, TX: 235,924 pounds
41. PROVIDENCE, RI: 232,701 pounds
42. BROWN, TX: 223,200 pounds
43. PAYETTE, ID: 220,095 pounds
44. LEE, AL: 219,349 pounds
45. MARION, AL: 211,600 pounds
46. VICTORIA, TX: 208,720 pounds
47. POLK, GA: 204,047 pounds
48. ST. LOUIS, MO: 203,273 pounds
49. FORSYTH, NC: 200,006 pounds
50. LOS ANGELES, CA: 193,509 pounds
51. GENESEE, MI: 189,046 pounds
52. JEFFERSON, AL: 188,566 pounds
53. COLORADO, TX: 185,754 pounds
54. HARDY, WV: 182,173 pounds
55. SANDUSKY, OH: 181,421 pounds
56. BLACKFORD, IN: 181,088 pounds
57. DE KALB, IN: 180,318 pounds
58. CLARK, IN: 178,335 pounds

59. MCLEOD, MN: 176,000 pounds
60. ROCKLAND, NY: 175,683 pounds
61. COWLITZ, WA: 172,503 pounds
62. KALKASKA, MI: 170,653 pounds
63. GASTON, NC: 169,292 pounds
64. AIKEN, SC: 168,000 pounds
65. ST. CHARLES, MO: 164,970 pounds
66. VERNON, MO: 163,700 pounds
67. BLACK HAWK, IA: 162,081 pounds
68. ALLEGHENY, PA: 160,598 pounds
69. BERKS, PA: 158,937 pounds
70. OKLAHOMA, OK: 150,994 pounds
71. COSHOCTON, OH: 149,856 pounds
72. MARION, IL: 149,462 pounds
73. HENRY, VA: 148,195 pounds
74. YOUNG, TX: 147,700 pounds
75. GILES, VA: 145,661 pounds
76. YORK, SC: 144,126 pounds
77. HARRISON, TX: 143,781 pounds
78. HARFORD, MD: 143,411 pounds
79. GUILFORD, NC: 142,014 pounds
80. SMYTH, VA: 138,967 pounds
81. ORANGEBURG, SC: 138,500 pounds
82. ANDERSON, SC: 138,390 pounds
83. WYANDOTTE, KS: 138,290 pounds
84. NOBLE, IN: 136,602 pounds
85. ROANE, WV: 135,126 pounds
86. NOBLE, OH: 134,443 pounds
87. BUCKS, PA: 133,661 pounds
88. CALDWELL, NC: 132,926 pounds
89. ORANGE, CA: 132,421 pounds
90. DOUGLAS, IL: 132,400 pounds
91. NEW MADRID, MO: 130,675 pounds

92. MIDDLESEX, NJ: 127,767 pounds
93. FRANKLIN, OH: 126,940 pounds
94. WAYNE, MI: 124,469 pounds
95. OAKLAND, MI: 123,689 pounds
96. PERRY, MO: 122,987 pounds
97. SURRY, NC: 122,111 pounds
98. PETERSBURG (CITY), VA: 121,303 pounds
99. ELKHART, IN: 118,970 pounds
100. MILWAUKEE, WI: 116,492 pounds

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Zip Codes with Reported Total Environmental Releases

of METHYL ETHYL KETONE (78-93-3) from the About The Chemicals section of Scorecard

---

Ranked by (select your ranking criteria)

Total environmental releases

in

Entire United States Go (explain)

1. 77701 (TX): 1,625,250 pounds
2. 39703 (MS): 1,540,000 pounds
3. 76305 (TX): 917,372 pounds
4. 97503 (OR): 897,100 pounds
5. 43608 (OH): 670,250 pounds
6. 46394 (IN): 652,340 pounds
7. 31709 (GA): 608,225 pounds
8. 36305 (AL): 589,150 pounds
9. 38834 (MS): 582,320 pounds
10. 24523 (VA): 500,000 pounds
11. 53589 (WI): 492,977 pounds
12. 27509 (NC): 473,200 pounds
13. 70601 (LA): 424,339 pounds
14. 38063 (TN): 380,000 pounds
15. 16373 (PA): 374,136 pounds
16. 28451 (NC): 351,000 pounds
17. 71109 (LA): 350,601 pounds
18. 44483 (OH): 348,869 pounds
19. 60426 (IL): 335,000 pounds
20. 16344 (PA): 318,884 pounds
21. 77536 (TX): 301,890 pounds
22. 22601 (VA): 287,874 pounds
23. 25430 (WV): 280,000 pounds
24. 98203 (WA): 278,244 pounds
25. 16749 (PA): 266,355 pounds

26. 46368 (IN): 261,112 pounds
27. 35405 (AL): 256,227 pounds
28. 17922 (PA): 247,640 pounds
29. 00767 (PR): 241,000 pounds
30. 71801 (AR): 238,756 pounds
31. 29303 (SC): 235,070 pounds
32. 76801 (TX): 223,200 pounds
33. 83619 (ID): 220,095 pounds
34. 36803 (AL): 219,349 pounds
35. 70805 (LA): 214,872 pounds
36. 35661 (AL): 214,083 pounds
37. 46506 (IN): 213,182 pounds
38. 35563 (AL): 211,600 pounds
39. 77901 (TX): 208,720 pounds
40. 30153 (GA): 198,301 pounds
41. 49512 (MI): 186,639 pounds
42. 26836 (WV): 182,173 pounds
43. 74107 (OK): 182,002 pounds
44. 27105 (NC): 181,606 pounds
45. 43420 (OH): 181,421 pounds
46. 47348 (IN): 181,088 pounds
47. 47130 (IN): 178,335 pounds
48. 55350 (MN): 176,000 pounds
49. 10962 (NY): 171,900 pounds
50. 98632 (WA): 171,623 pounds
51. 49646 (MI): 170,653 pounds
52. 78962 (TX): 168,008 pounds
53. 29829 (SC): 168,000 pounds
54. 64772 (MO): 163,700 pounds
55. 50703 (IA): 162,081 pounds
56. 46706 (IN): 157,618 pounds
57. 77640 (TX): 156,800 pounds
58. 43812 (OH): 149,856 pounds

59. 62801 (IL): 149,462 pounds
60. 76450 (TX): 147,700 pounds
61. 67210 (KS): 147,000 pounds
62. 29730 (SC): 144,126 pounds
63. 21078 (MD): 143,411 pounds
64. 02919 (RI): 139,959 pounds
65. 19543 (PA): 139,668 pounds
66. 24354 (VA): 138,967 pounds
67. 29115 (SC): 138,000 pounds
68. 29625 (SC): 137,139 pounds
69. 35660 (AL): 136,168 pounds
70. 25276 (WV): 135,126 pounds
71. 43724 (OH): 134,443 pounds
72. 61919 (IL): 132,400 pounds
73. 63873 (MO): 130,675 pounds
74. 48439 (MI): 129,046 pounds
75. 46701 (IN): 128,128 pounds
76. 63775 (MO): 122,987 pounds
77. 24089 (VA): 120,616 pounds
78. 28056 (NC): 120,000 pounds
79. 43612 (OH): 119,144 pounds
80. 28633 (NC): 118,648 pounds
81. 15144 (PA): 118,605 pounds
82. 77522 (TX): 118,524 pounds
83. 98034 (WA): 115,000 pounds
84. 24124 (VA): 112,143 pounds
85. 73145 (OK): 112,000 pounds
86. 55414 (MN): 110,732 pounds
87. 01075 (MA): 109,025 pounds
88. 25401 (WV): 108,953 pounds
89. 18629 (PA): 106,012 pounds
90. 38901 (MS): 105,509 pounds
91. 23804 (VA): 104,477 pounds

92. 44102 (OH): 103,905 pounds
93. 47001 (IN): 103,420 pounds
94. 42348 (KY): 103,002 pounds
95. 28621 (NC): 101,607 pounds
96. 63043 (MO): 100,189 pounds
97. 77055 (TX): 99,307 pounds
98. 28105 (NC): 98,790 pounds
99. 63376 (MO): 98,570 pounds
100. 75606 (TX): 96,581 pounds

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Facilities with Reported Total Environmental Releases

of METHYL ETHYL KETONE (78-93-3) from the About the Chemicals section of Scorecard

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Ranked by (select your ranking criteria)

Total environmental releases
in
Entire United States
from
All reporting sectors
Go (explain)

1. MOBIL OIL BEAUMONT REFY., BEAUMONT, TX: 1,625,000 Pounds
2. GENCORP, COLUMBUS, MS: 1,540,000 Pounds
3. TEXAS RECREATION CORP., WICHITA FALLS, TX: 917,372 Pounds
4. IMATION ENTERPRISES CORP., WHITE CITY, OR: 897,100 Pounds
5. TEXTILEATHER CORP., TOLEDO, OH: 670,250 Pounds
6. AMOCO OIL CO., WHITING REFY., WHITING, IN: 652,340 Pounds
7. SONY MAGNETIC PRODS. INC. OF AMERICA, DOTHAN, AL: 589,150 Pounds
8. IPC CORINTH DIV. INC., CORINTH, MS: 582,320 Pounds
9. RUBATEX CORP. PLANT2, BEDFORD, VA: 500,000 Pounds
10. UNIROYAL ENGINEERED PRODS., STOUGHTON, WI: 492,977 Pounds
11. ATHOL CORP., BUTNER, NC: 473,200 Pounds
12. CITGO PETROLEUM CORP., LAKE CHARLES, LA: 421,919 Pounds
13. ALLIEDSIGNAL/ASTOR CORP., EMLENTON, PA: 374,136 Pounds
14. TEXTRON AUTOMOTIVE CO., AMERICUS, GA: 360,110 Pounds
15. TECHNICAL COATING INTL. INC., LELAND, NC: 351,000 Pounds
16. PENNZOIL-QUAKER STATE CO. SHREVEPORT REFY., SHREVEPORT, LA: 350,601 Pounds
17. ALCAN ALUMINUM CORP., WARREN, OH: 347,639 Pounds
18. ALLIED TUBE & CONDUIT CORP., HARVEY, IL: 335,000 Pounds
19. PENNZOIL-QUAKER STATE CO. ROUSEVILLE REFY. & PACKAGING, ROUSEVILLE, PA: 318,884 Pounds
20. O'SULLIVAN CORP., WINCHESTER, VA: 287,874 Pounds
21. IMATION ENTS. CORP. MIDDLEWAY PLANT PLANT, KEARNEYSVILLE, WV: 280,000 Pounds

22. BOEING COMMERCIAL AIRPLANE GROUP - EVERETT, EVERETT, WA: 278,244 Pounds
23. ALLIED-SIGNAL ASTOR CORP. MCKEAN PLANT, SMETHPORT, PA: 266,355 Pounds
24. SHELL CHEMICAL CO. DEER PARK, DEER PARK, TX: 266,231 Pounds
25. SEQUA COATINGS CORP., PRECOAT METALS DIV., PORTAGE, IN: 261,112 Pounds
26. JVC MAGNETICS AMERICA CO., TUSCALOOSA, AL: 256,227 Pounds
27. WOODGRAIN MILLWORK INC., AMERICUS, GA: 248,115 Pounds
28. GENCORP/AUBURN PLANT, AUBURN, PA: 247,640 Pounds
29. PUERTO RICO SUN OIL CO., YABUCOA, PR: 241,000 Pounds
30. BRENTWOOD IND. INC., HOPE, AR: 238,635 Pounds
31. REXAM INC. CUSTOM DIV., SPARTANBURG, SC: 235,070 Pounds
32. 3M CO., BROWNWOOD, TX: 223,200 Pounds
33. WOODGRAIN MILLWORK INC., MILLWORK & PREFINISH DIVISIONS, FRUITLAND, ID: 220,095 Pounds
34. QUANTEGY INC., OPELIKA, AL: 219,349 Pounds
35. REYNOLDS METALS CO. - ALLOYS PLANT, MUSCLE SHOALS, AL: 214,083 Pounds
36. BREMEN CORP., BREMEN, IN: 213,182 Pounds
37. 3M, GUIN, AL: 211,600 Pounds
38. DU PONT VICTORIA PLANT, VICTORIA, TX: 207,900 Pounds
39. ENGINEERED FABRICS CORP., ROCKMART, GA: 198,301 Pounds
40. SR OF TENNESSEE, RIPLEY, TN: 193,950 Pounds
41. TENNESSEE ELECTROPLATING, RIPLEY, TN: 186,050 Pounds
42. AMERICAN WOODMARK CORP., MOOREFIELD, WV: 182,173 Pounds
43. AEROQUIP INOAC CO., FREMONT, OH: 181,421 Pounds
44. 3M, HARTFORD CITY PLANT, HARTFORD CITY, IN: 181,088 Pounds
45. EXXON CO. USA BATON ROUGE REFY., BATON ROUGE, LA: 179,471 Pounds
46. 3M HUTCHINSON, HUTCHINSON, MN: 176,000 Pounds
47. PAXAR CORP., ORANGEBURG, NY: 171,900 Pounds
48. WEYERHAEUSER CO., LONGVIEW, WA: 171,623 Pounds
49. ITW CODING PRODS., KALKASKA, MI: 170,653 Pounds
50. R. J. REYNOLDS TOBACCO CO., WINSTON-SALEM, NC: 170,006 Pounds

51. UTEX IND. INC., WEIMAR, TX: 168,008 Pounds
52. AVONDALE MILLS INC.-WOODHEAD, GRANITEVILLE, SC: 168,000 Pounds
53. SUNOCO INC., TULSA, OK: 163,706 Pounds
54. 3M NEVADA PLANT, NEVADA, MO: 163,700 Pounds
55. QUALITY MAT CO. INC., WATERLOO, IA: 162,081 Pounds
56. MOTIVA PORT ARTHUR REFY., PORT ARTHUR, TX: 156,800 Pounds
57. BOEING CO. - WICHITA DIV., WICHITA, KS: 147,000 Pounds
58. CYTEC FIBERITE INC., HAVRE DE GRACE, MD: 143,411 Pounds
59. TEXAS RECREATION CORP., GRAHAM, TX: 140,300 Pounds
60. REXAM DSI, JOHNSTON, RI: 139,959 Pounds
61. CHIYODA AMERICA INC., MORGANTOWN, PA: 139,668 Pounds
62. DECOLAM INC., ORANGEBURG, SC: 138,000 Pounds
63. VYTECH IND. INC., ANDERSON, SC: 137,139 Pounds
64. REYNOLDS METALS CO. - SHEFFIELD PLANT, SHEFFIELD, AL: 136,168 Pounds
65. BF GOODRICH AEROSPACE, SPENCER, WV: 135,126 Pounds
66. INTERNATIONAL CONVERTER INC., CALDWELL, OH: 134,443 Pounds
67. CELANESE ACETATE L.L.C. CELRIVER PLANT, ROCK HILL, SC: 132,724 Pounds
68. FABRIONICS INC., CAMARGO, IL: 132,400 Pounds
69. VEMCO INC., GRAND BLANC, MI: 129,046 Pounds
70. DEXTER AXLE CO., ALBION, IN: 128,128 Pounds
71. TG USA CORP., PERRYVILLE, MO: 122,987 Pounds
72. COURTAULDS PERFORMANCE FILMS INC. PLANT II, FIELDALE, VA: 120,616 Pounds
73. RANCH IND., GASTONIA, NC: 120,000 Pounds
74. CROWN CORK & SEAL CO. INC., TOLEDO, OH: 119,144 Pounds
75. MARION COMPOSITES, MARION, VA: 119,000 Pounds
76. PPG INDS. INC. SPRINGDALE COMPLEX, SPRINGDALE, PA: 118,605 Pounds
77. EXXON BAYTOWN REFY., BAYTOWN, TX: 117,022 Pounds
78. AMERICAN MILLWORK INC., KIRKLAND, WA: 115,000 Pounds
79. CELANESE ACETATE - CELCO PLANT, NARROWS, VA: 112,143 Pounds
80. U.S. AIR FORCE, TINKER AIR FORCE BASE, OKLAHOMA CITY, OK: 112,000 Pounds

81. RIEKE CORP., AUBURN, IN: 111,618 Pounds
82. AMERICAN NATL. CAN CO. - PPMM, MINNEAPOLIS, MN: 110,732 Pounds
83. SWAN CORP., CENTRALIA, IL: 110,516 Pounds
84. STONE CONTAINER CORP., COSHOCTON, OH: 110,181 Pounds
85. REXAM GRAPHICS, SOUTH HADLEY, MA: 109,025 Pounds
86. BRENTWOOD INDS. INC., MARTINSBURG, WV: 108,953 Pounds
87. PROCTER & GAMBLE PAPER PRODS. CO., MEHOOPANY, PA: 106,012 Pounds
88. HEATCRAFT INC., GRENADA, MS: 105,509 Pounds
89. BRENCO INC., PETERSBURG, VA: 104,477 Pounds
90. AMERICAN NATL. CAN CO. - PPCO, CLEVELAND, OH: 103,905 Pounds
91. AURORA CASKET CO. INC., AURORA, IN: 103,420 Pounds
92. ARVIN ROLL COATER HAWESVILLE FACILITY, HAWESVILLE, KY: 103,002 Pounds
93. TRANSFORMER MATERIALS CO., MARYLAND HEIGHTS, MO: 99,070 Pounds
94. REXAM INC., CUSTOM DIV., MATTHEWS, NC: 98,790 Pounds
95. TRANSFORMER MATERIALS CO., SAINT PETERS, MO: 98,570 Pounds
96. PLASTENE SUPPLY CO., PORTAGEVILLE, MO: 98,180 Pounds
97. KITCHEN KOMPACT, JEFFERSONVILLE, IN: 98,000 Pounds
98. STEMCO INC., LONGVIEW, TX: 96,581 Pounds
99. AMERICAN REFINING GROUP INC., BRADFORD, PA: 96,000 Pounds
100. KEN-KOAT INC., HUNTINGTON, IN: 92,731 Pounds

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Industrial Sectors with Reported Total Environmental Releases

of METHYL ETHYL KETONE (78-93-3) by Industrial Sector (2-digit SIC) from the About the Chemicals section of Scorecard

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Ranked by (select your ranking criteria)

Total environmental releases

in

Entire United States Go (explain)

1. 30: Rubber And Misc. Plastics Products : 8,561,319 pounds
2. 37: Transportation Equipment : 5,731,434 pounds
3. 29: Petroleum And Coal Products : 5,336,062 pounds
4. 34: Fabricated Metal Products : 4,557,156 pounds
5. 22: Textile Mill Products : 3,959,913 pounds
6. 28: Chemicals And Allied Products : 3,683,710 pounds
7. 26: Paper And Allied Products : 3,211,672 pounds
8. 36: Electronic & Other Electric Equipment : 1,672,577 pounds
9. 24: Lumber And Wood Products : 1,620,634 pounds
10. 33: Primary Metal Industries : 1,332,806 pounds
11. 35: Industrial Machinery And Equipment : 1,183,339 pounds
12. 38: Instruments And Related Products : 1,182,495 pounds
13. 39: Miscellaneous Manufacturing Industries : 1,152,016 pounds
14. 25: Furniture And Fixtures : 1,143,512 pounds
15. 27: Printing And Publishing : 890,564 pounds
16. 32: Stone, Clay, And Glass Products : 425,641 pounds
17. 97: National Security And Intl. Affairs : 412,623 pounds
18. 31: Leather And Leather Products : 315,222 pounds
19. 21: Tobacco Products : 179,406 pounds
20. 51: Wholesale Trade--Nondurable Goods : 168,910 pounds
21. 17: Special Trade Contractors : 125,125 pounds
22. 49: Electric, Gas, And Sanitary Services : 86,538 pounds
23. NA: Not reported : 66,268 pounds
24. 23: Apparel And Other Textile Products : 54,214 pounds

25. 73: Business Services : 17,918 pounds
26. 87: Engineering & Management Services : 9,953 pounds
27. 45: Transportation By Air : 8,800 pounds
28. 96: Administration Of Economic Programs : 7,963 pounds
29. 20: Food And Kindred Products : 4,647 pounds
30. 76: Miscellaneous Repair Services : 3,778 pounds
31. 42: Trucking And Warehousing : 10 pounds

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Regulatory Coverage

of METHYL ETHYL KETONE (78-93-3) from Scorecard

Federal Regulatory Program Lists

- Air Contaminants (Occupational and Safety Health Act)
- Hazardous Air Pollutants (Clean Air Act)
- Hazardous Constituents (Resource Conservation and Recovery Act)
- Hazardous Substances (Superfund)
- Toxic Release Inventory Chemicals

California State Regulatory Program Lists

- California Air Toxics "Hot Spots" Chemicals (Assembly Bill 2588)
- California Toxic Air Contaminants (Assembly Bill 1807)

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Basic Testing to Identify Chemical Hazards

for METHYL ETHYL KETONE (78-93-3) from Scorecard

The U.S. EPA conducted a comprehensive review of publicly available chemical testing data in 1997 to examine whether the basic information needed to identify chemical hazards is available for high production volume chemicals. EPA searched major chemical databases to determine if the following tests had been conducted on a chemical:

- Acute toxicity
- Chronic toxicity
- Neurotoxicity
- Developmental or reproductive toxicity
- Mutagenicity
- Carcinogenicity
- Ecotoxicity
- Environmental fate

The following basic tests to identify chemical hazards have either not been conducted or are not publicly available:

- Carcinogenicity

More on the importance of basic toxicity testing

Reference

EPA. Chemical Hazard Data Availability Study: High Production Volume (HPV) Chemicals and SIDS Testing
Office of Pollution Prevention and Toxics, EPA,Washington, DC. 1998.

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Safety Assessment Data

for METHYL ETHYL KETONE (78-93-3) from Scorecard

Are Risk Assessment Values Available?

Health Risk of Concern	Inhalation	Ingestion
Cancer	Not a recognized carcinogen	Not a recognized carcinogen
Noncancer	Yes	Yes

Are Exposure Data Available?

Type of Exposure	
Inhalation - ambient air	Monitoring data available in some states
Inhalation - indoor air	**No**
Ingestion	**No**

- See the data US EPA possesses for safety assessment.

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Scorecard Risk Characterization Data

for METHYL ETHYL KETONE (78-93-3) from Scorecard

Risk Assessment Values or Standards

	Value	Units	Reference
Inhalation cancer risk value (potency)	Not a recognized or suspect carcinogen		
Inhalation noncancer risk value (reference concentration)	10000	ug/m3	OEHHA99-REL
National ambient air quality standard	Gap in regulatory coverage		
Ingestion cancer risk value (potency)	Not a recognized or suspect carcinogen		
Ingestion noncancer risk value (reference dose)	0.6	mg/kg-day	IRIS-HEAST
National water quality standard	7.5	mg/L	EPA-HA

See the data US EPA possesses for safety assessment.

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Chemical Classes

for METHYL ETHYL KETONE (78-93-3) from Scorecard

Note that METHYL ETHYL KETONE may be a member of the following classes:

- VOLATILE ORGANIC COMPOUNDS

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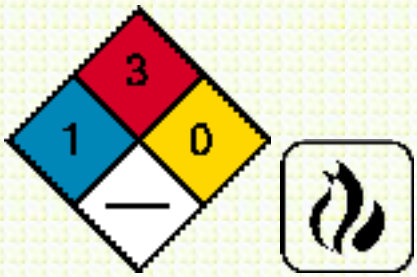
ToxFAQs

2-Butanone

CAS# 78-93-3

September 1995

2-Butanone
C_4H_8O
Stereo Image
XYZ File



NFPA Label Key

Material Safety Data Sheet
(University of Utah)

Agency for Toxic Substances and Disease Registry

This fact sheet answers the most frequently asked health questions about 2-butanone. For more information, you may call the ATSDR Information Center at 1-800-447-1544. This fact sheet is one in a series of summaries about hazardous substances and their health effects. This information is important because this substance may harm you. The effects of exposure to any hazardous substance depend on the dose, the duration, how you are exposed, personal traits and habits, and whether other chemicals are present.

SUMMARY: Exposure to 2-butanone occurs in the workplace or from using consumer products containing it. Mild irritations of the eyes, nose, and throat were seen in people who breathed 2-butanone. This chemical has been found in at least 472 of 1,416 National Priorities List sites identified by the Environmental Protection Agency.

What is 2-butanone?
(Pronounced 2-byoo'ta-no-n)

2-Butanone is a manufactured chemical but it is also present in the environment from natural sources. It is a colorless liquid with a sharp, sweet odor. It is also known as methyl ethyl ketone (MEK).

2-Butanone is produced in large quantities. Nearly half of its use is in paints and other coatings because it will quickly evaporate into the air and it dissolves many substances. It is also used in glues and as a cleaning agent.

2-Butanone occurs as a natural product. It is made by some trees and found in some fruits and vegetables in small amounts. It is also released to the air from car and truck exhausts.

What happens to 2-butanone when it enters the environment?

- 2-Butanone enters the air during production, use and transport, and from hazardous waste sites.
- In air, one-half of it will break down from sunlight in 1 day or less.
- It dissolves in water and is broken down more slowly to a simpler chemical form in about 2 weeks.
- It does not stick to soil and will travel through the soil to the groundwater.
- Some of the 2-butanone in soil or water will evaporate into the air.
- It does not deposit in the bottom of rivers or lakes.
- It is not expected to concentrate in fish or increase in the tissues of animals further up the food chain.

How might I be exposed to 2-butanone?

- Breathing contaminated air from the production or use of paints, glues, coatings, or cleaning agents containing it
- Breathing contaminated air near hazardous waste sites
- Breathing cigarette smoke
- Sniffing glues
- Drinking contaminated water from wells near manufacturing or hazardous waste sites
- Skin contact with the liquid during production or use.

How can 2-butanone affect my health?

The known health effects to people from exposure to 2-butanone are irritation of the nose, throat, skin, and eyes. No one has died from breathing 2-butanone alone. If 2-butanone is breathed along with other chemicals that damage health, it can increase the amount of damage that occurs.

Serious health effects in animals have been seen only at very high levels. When breathed, these effects included birth defects, loss of consciousness, and death.

When swallowed, rats had nervous system effects including drooping eyelids and uncoordinated muscle movements. There was no damage to the ability to reproduce.

Mice who breathed low levels for a short time showed temporary behavioral effects. Mild kidney damage was seen in animals that drank water with lower levels of 2-butanone for a short time.

There are no long-term studies with animals either breathing or drinking 2-butanone.

How likely is 2-butanone to cause cancer?

The Department of Health and Human Services has not classified 2-butanone as to its human

carcinogenicity.

The International Agency for Research on Cancer and the Environmental Protection Agency (EPA) have also not classified 2-butanone as to its human carcinogenicity.

Two studies of workers exposed to 2-butanone and other chemicals did not find an increase in cancer. No animal studies are available that examine the potential for 2-butanone to cause cancer.

Is there a medical test to show whether I've been exposed to 2-butanone?

Tests are available to measure 2-butanone or its breakdown products in blood, breath, and urine. These tests are useful only to measure recent exposures because 2-butanone and its breakdown products leave the body rapidly. These tests are not usually performed at your doctor's office, but your doctor can take blood or urine samples and send them to a testing laboratory.

Has the federal government made recommendations to protect human health?

The EPA requires that discharges or spills into the environment of 5,000 pounds of more of 2-butanone be reported.

The Occupational Safety and Health Administration (OSHA) set an occupational exposure limit of 200 parts of 2-butanone per million parts of workplace air (200 ppm) for an 8-hour workday, 40-hour workweek.

The American Conference of Governmental Industrial Hygienists (ACGIH) and the National Institute for Occupational Safety and Health (NIOSH) have established the same guidelines as OSHA for the workplace.

Glossary

Carcinogenicity:

Ability to cause cancer.

Evaporate:

To change into a vapor or a gas.

PPM:

Parts per million.

Long-term:

Lasting one year or longer.

Short time:

Lasting 14 days or less.

References

Agency for Toxic Substances and Disease Registry (ATSDR). 1992. Toxicological profile for 2-butanone. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service.

Where can I get more information?

ATSDR can tell you where to find occupational and environmental health clinics. Their specialists can

recognize, evaluate, and treat illnesses resulting from exposure to hazardous substances. You can also contact your community or state health or environmental quality department if you have any more questions or concerns.

For more information, contact:

Agency for Toxic Substances and Disease Registry
Division of Toxicology
1600 Clifton Road NE, Mailstop E-29
Atlanta, GA 30333
Phone: 1-800-447-1544
FAX: 404-639-6315



U.S. Department of Health and Human Services
Public Health Service
Agency for Toxic Substances and Disease Registry

Link to ToxFAQs Home Page

Link to ATSDR Science Corner

Link to ATSDR Home Page

METHYL ETHYL KETONE

Methyl ethyl ketone is a federal hazardous air pollutant and was identified as a toxic air contaminant in April 1993 under AB 2728.

CAS Registry Number: 78-93-3

Structure: $C_2H_5COCH_3$

Molecular Formula: C_4H_8O

Description

Methyl ethyl ketone is a flammable, colorless liquid with an acetone-like, sweet, pungent odor. It is soluble in four parts water and miscible with alcohol, ether, acetone, and benzene. It is lighter than water and may be expected to float while rapidly dissolving (HSDB, 1991).

Physical Properties of Methyl Ethyl Ketone

Molecular Weight	72.10
Boiling Point	79.6 oC
Melting Point	-86.35 oC
Flash Point:	-6 oC (21 oF) (closed cup)
Vapor Pressure	90.6 mm Hg at 25 oC
Vapor Density	2.41 (air = 1)
Density/Specific Gravity	0.805 at -20/4 oC (water = 1)
Log/Octanol Partition Coefficient	0.29
Henry's Law Constant	1.05 x 10-5 atm-m3/mole
Conversion Factor	1 ppm = 2.95 mg/m3

(HSDB, 1991; Merck, 1989; Sax, 1989; U.S. EPA, 1994a)

SOURCES AND EMISSIONS

A. Sources

Methyl ethyl ketone is used as a solvent for lacquers, adhesives, rubber cement, printing inks, and paint removers, in cleaning solutions, as a catalyst, and as a carrier. Cigarette smoke and gasoline exhaust are also sources of methyl ethyl ketone. Methyl ethyl ketone has been detected or quantified in motor vehicle exhaust by the Air Resources Board (ARB) (ARB, 1995e).

The primary stationary sources that have reported emissions of methyl ethyl ketone in California are

millwork, veneer, and plywood manufacturers, manufacturers of wood furniture, and manufacturers of rubber and plastic footwear (ARB, 1997b).

B. Emissions

The total emissions of methyl ethyl ketone from stationary sources in California are estimated to be at least 290,000 pounds per year, based on data reported under the Air Toxics "Hot Spots" Program (AB 2588) (ARB, 1997b).

C. Natural Occurrence

Methyl ethyl ketone occurs naturally in volcanos, forest fires, products of biological degradation, and is a natural component of food (Howard, 1990).

AMBIENT CONCENTRATIONS

Methyl ethyl ketone is routinely monitored by the Air Resources Board statewide air toxics network. The network's mean concentration of methyl ethyl ketone from January 1996 to December 1996 is estimated to be 0.32 micrograms per cubic meter (µg/m3) or 0.11 parts per billion (ppb) (ARB, 1997c).

The United States Environmental Protection Agency (U.S. EPA) has also compiled ambient concentration data for methyl ethyl ketone from several locations throughout the United States from 1972-87. A mean ambient concentration of 1.4 µg/m3 (0.47 ppb) was derived from these data (U.S. EPA, 1993a).

INDOOR SOURCES AND CONCENTRATIONS

No information about the indoor sources and concentrations of methyl ethyl ketone was found in the readily-available literature.

ATMOSPHERIC PERSISTENCE

If released to the atmosphere, methyl ethyl ketone will exist primarily in the gas phase. The dominant tropospheric loss process of methyl ethyl ketone appears to be reaction with the hydroxyl (OH) radical, with photolysis being unimportant. The calculated half-life and lifetime of methyl ethyl ketone due to reaction with the OH radical are 9 days and 13 days, respectively. The products of the OH radical reaction are acetaldehyde, formaldehyde and, in the presence of nitrogen dioxide (NO2), peroxyacetyl nitrate (PAN) (Atkinson, 1994).

AB 2588 RISK ASSESSMENT INFORMATION

Although methyl ethyl ketone is reported as being emitted in California from stationary sources no health values (cancer or non-cancer) are listed in the California Air Pollution Control Officers Association Air

Toxics "Hot Spots" Program Revised 1992 Risk Assessment Guidelines for use in risk assessments (CAPCOA, 1993).

HEALTH EFFECTS

Probable routes of human exposure to methyl ethyl ketone are inhalation, ingestion, and dermal contact (Sittig, 1991).

Non-Cancer: Exposure to methyl ethyl ketone vapors can cause eyes, nose, throat, and respiratory tract irritation. Methyl ethyl ketone is a central nervous system depressant. Methyl ethyl ketone enhances the neurotoxicity of n-hexane (U.S. EPA, 1994a).

The U.S. EPA has established a Reference Concentration (RfC) of 1.0 milligram per cubic meter for methyl ethyl ketone, based on decreased fetal birth weight in mice. The U.S. EPA estimates that inhalation of this concentration or less, over a lifetime, would not likely result in the occurrence of chronic, non-cancer effects. The U.S. EPA has established an oral Reference Dose (RfD) for methyl ethyl ketone of 0.6 milligrams per kilogram per day, based on decreased fetal birth weights in rats. The U.S. EPA estimates that consumption of this dose or less, over a lifetime, would not likely result in the occurrence of chronic, non-cancer effects (U.S. EPA, 1994a).

No information was located on adverse reproductive effects of methyl ethyl ketone in humans. Retardation of fetal development and fetal malformations were reported in mice exposed to methyl ethyl ketone by inhalation (U.S. EPA, 1994a).

Cancer: No information is available regarding carcinogenic effects in humans from exposure to methyl ethyl ketone. The U.S. EPA has placed methyl ethyl ketone in Group D: Not classifiable as a carcinogen, based on lack of data in humans and animals (U.S. EPA, 1994a). The International Agency for Research on Cancer has not classified methyl ethyl ketone for carcinogenicity (IARC, 1987a).

EPA United States Environmental Protection Agency
Office of Air Quality Planning & Standards OAQPS
TTNWeb Technology Transfer Network
UATW Unified Air Toxics Website

METHYL ETHYL KETONE

Hazard Summary

CAUTION: Unless otherwise noted, the quantitative information on these fact sheets are from "EPA Health Effects Notebook for Hazardous Air Pollutants-Draft", EPA-452/D-95-00, PB95-503579, December 1994." Please conduct a current literature search and check the appropriate current online database for the most recent quantitative information.

- Acute (short-term) exposure to methyl ethyl ketone in humans, via inhalation, results in **irritation to the eyes, nose, and throat, and central nervous system depression.**
- Limited information is available on the chronic (long-term) effects of methyl ethyl ketone in humans. Chronic inhalation studies in animals have reported effects on the central nervous system, liver, and respiratory system.
- The Reference Concentration (RfC) for methyl ethyl ketone is 1.0 mg/m^3.[a] The U.S. Environmental Protection Agency (EPA) estimates that inhalation of this concentration or less, over a lifetime, would not likely result in the occurrence of chronic, noncancer effects.[b]
- The Reference Dose (RfD) for methyl ethyl ketone is 0.6 mg/kg/d.[c] EPA estimates that consumption of this level or less, over a lifetime, would not likely result in the occurrence of chronic, noncancer effects.
- No information is available on the developmental or reproductive effects of methyl ethyl ketone in humans. **Reduction of fetal development and fetal malformations** has been reported in mice exposed to methyl ethyl ketone in the air.
- Limited data are available on the carcinogenic effects of methyl ethyl ketone. No human data are available and the only available animal study did not report skin tumors from dermal exposure to methyl ethyl ketone. EPA has classified methyl ethyl ketone as a Group D, **not classifiable as to human carcinogenicity.**

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[a] Milligrams per cubic meter is the unit of measurement for chemicals in air.

[b] The RfC is not a direct estimator of risk, but rather a reference point to gauge the potential effects. Exceedance of the RfC does not imply that an adverse health effect would necessarily occur. As the amount and frequency of exposures exceeding the RfC increase, the probability that adverse health effects may be seen also increases.

[c] Milligrams per kilogram per day is one way to measure the amount of the contaminant that is consumed in food.

Please Note: The main sources of information for this fact sheet are EPA's *Health Effects Assessment for Methyl Ethyl Ketone* and EPA's Integrated Risk Information System (IRIS), which contains information on inhalation chronic toxicity of methyl ethyl ketone and the RfC and oral chronic toxicity and the RfD. Other secondary sources include the Hazardous Substances Data Bank (HSDB), a database of summaries of peer-reviewed literature, and the Registry of Toxic Effects of Chemical Substances (RTECS), a database of toxic effects that are not peer reviewed.

Environmental/Occupational Exposure

- Methyl ethyl ketone has been detected in both indoor and outdoor air. Methyl ethyl ketone can be produced in outdoor air by the photooxidation of certain air pollutants, such as butane and other hydrocarbons. (1)
- Methyl ethyl ketone has been found in drinking water and surface water at a number of sites. (2)
- Exposure to methyl ethyl ketone could also occur at the workplace and through exposure to household products containing the chemical. (1)

Assessing Personal Exposure

- Levels of methyl ethyl ketone in the urine can be measured to determine exposure to the chemical. (1)

Health Hazard Information

Acute Effects:

- Acute exposure to high concentrations of methyl ethyl ketone in humans produces irritation to the eyes, nose, and throat. (1,3,4)
- Other effects reported from acute inhalation exposure in humans include central nervous system depression, headache, and nausea. (1,3,4)
- Dermatitis has been reported in humans following dermal exposure to methyl ethyl ketone. (1)
- Tests involving acute exposure of animals, such as the LD_{50} test in rabbits, has shown methyl ethyl ketone to have high acute toxicity from dermal exposure, while the LD_{50} test in rats and mice has shown the chemical to have moderate toxicity from ingestion. (5)
- The LC_{50} test in rats has indicated low toxicity from methyl ethyl ketone exposure via inhalation. (5)

Chronic Effects (Noncancer):

- Limited information is available on the chronic effects of methyl ethyl ketone in humans from inhalation exposure. One study reported nerve damage in individuals who sniffed a glue thinner containing methyl ethyl ketone and other chemicals. (1)

- Slight effects on the central nervous system, liver, and respiratory system have been reported in chronic inhalation studies of methyl ethyl ketone in animals. (1)
- The RfC for methyl ethyl ketone is 1 mg/m^3 based on decreased fetal birth weight in mice. (6)
- EPA has medium confidence in the principal study on which the RfC is based because it is well designed and tested several exposure concentrations and several endpoints of toxicity although there are insufficient data presented for possible respiratory effects; low confidence in the database because there are no multigenerational studies and only one subchronic study and portal-of-entry effects are not adequately address; and, consequently, confidence in the RfC is low. (6)
- The RfD for methyl ethyl ketone is 0.6 mg/kg/d based on decreased fetal birth weight in rats. (6)
- EPA has low confidence in the study on which the RfD is based because lowering the high-dose group from 3.0 to 2.0% confounded determination of the critical effect; low confidence in the database because of the lack of oral data for MEK itself and the absence of data in a second species; and, consequently, low confidence in the RfD. (6)
- EPA's Office of Air Quality Planning and Standards, for a hazard ranking under Section 112(g) of the Clean Air Act Amendments, has evaluated methyl ethyl ketone for chronic toxicity and has given it a composite score of 10 (scores range from 1 to 100, with 100 being the most toxic). These scores are nonlinear and are the product of two ratings: a rating based on the minimal-effect dose and a rating based on the type of effect. (9)

Reproductive/Developmental Effects:

- No information on the reproductive or developmental effects of methyl ethyl ketone in humans was located.
- An inhalation study in mice reported retardation of fetal development and fetal malformations in animals exposed to methyl ethyl ketone. (4)

Cancer Risk:

- No information on the carcinogenicity of methyl ethyl ketone in humans was located.
- No studies were available on the carcinogenicity of methyl ethyl ketone by the oral or inhalation routes. In a dermal carcinogenicity study, skin tumors were not reported from methyl ethyl ketone exposure. (1,6)
- EPA has classified methyl ethyl ketone as a Group D, not classifiable as to human carcinogenicity, based on a lack of data concerning carcinogenicity in humans and animals. (6)

Physical Properties

- Methyl ethyl ketone is a colorless volatile liquid that is soluble in water. (2)
- The odor threshold for methyl ethyl ketone is 5.4 ppm, with an acetone-like odor reported. (8)
- The chemical formula for methyl ethyl ketone is C_4H_8O and the molecular weight is 72.10 g/mol. (9)
- The vapor pressure for methyl ethyl ketone is 95.1 mm Hg at 25 C, and it has a log octanol/water partition coefficient (Log K_{ow}) of 0.261. (9)

Uses

- The primary use of methyl ethyl ketone is as a solvent in processes involving gums, resins, cellulose acetate, and cellulose nitrate. (1)
- Methyl ethyl ketone is also used in the synthetic rubber industry, in the production of paraffin wax, and in household products such as lacquer and varnishes, paint remover, and glues. (1)

Conversion Factors:
To convert from ppm to mg/m^3: mg/m^3 = (ppm) × (molecular weight of the compound)/(24.45). For methy ethyl ketone: 1 ppm = 2.95 mg/m^3.

Health Data from Inhalation Exposure

Concentration (mg/m^3)	Health numbers[a]	Regulatory, advisory numbers[b]	Reference
100,000.0			
-- -- -- -- 10,000.0	• LC_{50} (rat) (23,500 mg/m^3)		5
-- -- -- -- 1,000.0	• LOAEL (mice) (8,906 mg/m^3)[c] • NOAEL (mice) (2,978 mg/m^3)[c]		6 6
-- -- -- -- 100.0		• OSHA PEL and ACGIH TLV (STEL) (885 mg/m^3) • OSHA PEL, ACGIH TLV, and NIOSH REL (590 mg/m^3)	3 3
-- -- -- -- 10.0			
-- -- -- -- 1.0	• RfC (1 mg/m^3)		6

ACGIH STEL--American Conference of Governmental and Industrial Hygienists' short-term exposure

limit: 15-min time-weighted-average exposure that should not be exceeded at any time during a workday even if the 8-h time-weighted-average is within the threshold limit value.
ACGIH TLV--American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.
LC_{50} (Lethal Concentration$_{50}$)--A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.
LOAEL--Lowest-observed-adverse-effect level.
NIOSH REL--National Institute of Occupational Safety and Health's recommended exposure limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling.
NOAEL--No-observed-adverse-effect level.
OSHA PEL--Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.
RfC--Reference concentration.

[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.
[c] The LOAEL and NOAEL are from the critical study used as the basis for the EPA RfC.

References

1. U.S. Environmental Protection Agency. *Updated Health Effects Assessment for Methyl Ethyl Ketone*. EPA/600/8-89/093. Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development, Cincinnati, OH. 1990.
2. U.S. Environmental Protection Agency. *Health Advisory for Methyl Ethyl Ketone.* Office of Drinking Water, Washington, DC. 1987.
3. E.J. Calabrese and E.M. Kenyon. *Air Toxics and Risk Assessment*. Lewis Publishers, Chelsea, MI. 1991.
4. U.S. Department of Health and Human Services. Hazardous Substances Data Bank (HSDB, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.
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6. U.S. Environmental Protection Agency. *Integrated Risk Information System (IRIS) on Methyl Ethyl Ketone*. Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development, Cincinnati, OH. 1993.
7. U.S. Environmental Protection Agency. *Technical Background Document to Support Rulemaking Pursuant to the Clean Air Act--Section 112(g). Ranking of Pollutants with Respect to Hazard to Human Health*. EPA-450/3-92-010. Emissions Standards Division, Office of Air Quality Planning and Standards, Research Triangle Park, NC. 1994.

8. J.E. Amoore and E. Hautala. Odor as an aid to chemical safety: Odor thresholds compared with threshold limit values and volatilities for 214 industrial chemicals in air and water dilution. *Journal of Applied Toxicology*, 3(6):272-290. 1983.
9. U.S. Environmental Protection Agency. Assessment Tools for the Evaluation of Risk (ASTER, online database). Environmental Research Laboratory, Duluth, MN. 1993.

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Methyl ethyl ketone (MEK)

CASRN 78-93-3

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0071
Methyl ethyl ketone (MEK); CASRN 78-93-3

Health assessment information on a chemical substance is included in IRIS only after a comprehensive review of chronic toxicity data by U.S. EPA health scientists from several Program Offices and the Office of Research and Development. The summaries presented in Sections I and II represent a consensus reached in the review process. Background information and explanations of the methods used to derive the values given in IRIS are provided in the Background Documents.

STATUS OF DATA FOR MEK

File On-Line 01/31/1987

Category (section)	Status	Last Revised
Oral RfD Assessment (I.A.)	on-line	05/01/1993
Inhalation RfC Assessment (I.B.)	on-line	07/01/1992

Carcinogenicity Assessment (II.) on-line 12/01/1989

_I. CHRONIC HEALTH HAZARD ASSESSMENTS FOR NONCARCINOGENIC EFFECTS

__I.A. REFERENCE DOSE FOR CHRONIC ORAL EXPOSURE (RfD)

Substance Name -- Methyl ethyl ketone (MEK)
CASRN -- 78-93-3
Last Revised -- 05/01/1993

The oral Reference Dose (RfD) is based on the assumption that thresholds exist for certain toxic effects such as cellular necrosis. It is expressed in units of mg/kg-day. In general, the RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. Please refer to the Background Document for an elaboration of these concepts. RfDs can also be derived for the noncarcinogenic health effects of substances that are also carcinogens. Therefore, it is essential to refer to other sources of information concerning the carcinogenicity of this substance. If the U.S. EPA has evaluated this substance for potential human carcinogenicity, a summary of that evaluation will be contained in Section II of this file.

___I.A.1. ORAL RfD SUMMARY

Critical Effect	Experimental Doses*	UF	MF	RfD
Decreased fetal birth weight	NOAEL: 1771 mg/kg-day (1% 2-butanol solution)	3000	1	6E-1 mg/kg-day
Multigeneration/ Developmental Rat Feeding Study	LOAEL: 3122 mg/kg-day (2% 2-butanol solution)			
Cox et al., 1975				

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*Conversion Factors and Assumptions: Based on actual consumption data for the

NOAEL and regression analysis for the LOAEL of exposure to 2-butanol, a metabolic intermediate of methyl ethyl ketone.

___I.A.2. PRINCIPAL AND SUPPORTING STUDIES (ORAL RfD)

Cox, G.E., D.E. Bailey and K. Morgareidge. 1975. Toxicity studies in rats with 2-butanol including growth, reproduction and teratologic observations. Food and Drug Research Laboratories, Inc., Waverly, NY, Report No. 91MR R 1673.

The identification of the critical effect for methyl ethyl ketone (MEK), also referred to as 2-butanone, is based on its metabolic intermediate, 2-butanol. A detailed rationale for use of this intermediate of MEK can be found in Additional Comments/Studies.

Weanling FDRL-Wistar stock rats (30/sex/group) were given 2-butanol in drinking water at 0, 0.3, 1.0, or 3.0% solutions and a standard laboratory ration ad libitum. Weekly feed, fluid intakes and body weights were recorded to determine the efficiency of food utilization and to calculate the average daily intake of 2-butanol. The average daily intake of 2-butanol for males was 0, 538, 1644, and 5089 mg/kg-day and for females was 0, 594, 1771, and 4571 mg/kg-day for the 0, 0.3, 1.0, and 3.0% solutions, respectively. At the highest exposure level (3.0%), net weight gain was reduced compared with controls both in males (229 g vs. 269 g in controls) and females (130 g vs. 154 g in controls) during the 8 weeks of initial monitoring. However, no differences were found in the efficiency of food utilization.

After 9 weeks of exposure, parental matings were made with one male and one female from each of the respective treatment groups (P generation). Following birth of the first litter (F1A) of the parental generation, various reproduction and lactation responses were measured. This study design incorporated a multigeneration protocol with measurement of developmental toxicity endpoints. Significant effects were noted in the litters from the 3.0% 2-butanol dose group vs. the control group, including the number of pups/litter cast alive (8.46 vs. 10.3), the number of pups/litter alive at 4 days before culling (8.12 vs. 10.3), the number of pups/litter alive at 21 days (6.85 vs. 7.68), the mean body weight/pup after culling at 4 days (8.2 g vs. 10.3 g) and the mean body weight/pup at 21 days (28.4 g vs. 49.5 g).

Based on results found in the 3.0% (high-dose) 2-butanol F1A generation, the treatment of all high-dose parents and offspring was reduced to 2.0% 2-butanol for the remainder of the experimental protocol. Following a 2-week interim adaptation period to allow the F1A generation animals to attain a more normal weight, the P generation was subsequently remated to produce a second litter (F1B), and the F1A generation selected for an F2 mating. Therefore, a new high dose of 2.0% 2-butanol was calculated to be equivalent to 3384 mg/kg-day in males and 3122 mg/kg-day in females based on regression analysis of the 8 week water intake data. The F1B litters receiving 2.0% 2-butanol showed a slight reduction in average fetal weight compared with controls (3.74 g vs. 4.14 g in controls). Nidation, early fetal deaths, and late fetal deaths were not detectably affected. Skeletal findings also were reported for the F1B

generation. The 2.0% group showed apparent increases in missing sternebrae, wavy ribs, and incomplete vertebrae ossification when compared with both the 0.3 and 1.0% groups. However, because of the rather high incidence in the control group for these findings, these effects could not be determined to be compound-related. The 2.0% group also showed a reduction in the mean body weight per pup at day 4 following culling (9.48 g vs. 10.0 g in the control) and in the mean body weight at 21 days (34.9 vs. 41.1 g in the control). Although these reductions were not as great in the high dose (3.0%) F1A generation, the percent body weight reduction in the F1B high dose (2.0%) was doubled at 21 days (reductions of 5% at 4 days and 11% at 21 days). This generation showed the same doubling trend in fetal weight reduction as was reported in the F1A group exposed to 3.0% 2-butanol throughout (reductions of 21% at 4 days and 43% at 21 days). These results are also presented in abstract form by Gallo et al. (1977).

At the 2.0% level of the F2 generation, there were a number of histopathologic changes noted in the kidney of the male rats only. These changes were characterized by nonreactive tubular degeneration in the outer medullary zone, tubular cast formation, foci of tubular degeneration and regeneration, microcysts in the renal papilla, glomerular fibrosis, and focal epithelial calcification. These findings are consistent with the pattern of early stages of alpha 2u-globulin-associated rat nephrotoxicity as set forth by the Risk Assessment Forum (U.S. EPA, 1991). As per the Agency's guidance, it is not appropriate to use these specie-and sex-specific renal effects to establish a critical effect.

Administration of 2-butanol resulted in the occurrence of developmental effects. Decreased pup survivability and fetal weight were seen in the 3.0% group, and in the F1 offspring (F1A and F1B, whose parents received 3.05 and 2.0% 2-butanol, respectively). The decrease in fetal weight continued to be demonstrated in the F2 generation at the 2.0% level. Therefore, based on these developmental toxicologic endpoints, a LOAEL of 3122 mg/kg-day (2.0% solution) and a NOAEL of 1771 mg/kg-day (1.0% solution) are identified.

___I.A.3. UNCERTAINTY AND MODIFYING FACTORS (ORAL RfD)

UF -- Four uncertainty factors of 10 each were applied, one to account for interspecies extrapolation and intraspecies variability (extrapolation to sensitive human populations); one to adjust for subchronic to chronic extrapolation since long-term effects in the dams during the exposure period were not reported in the principal study; one for incompleteness of the data base, including a lack of both subchronic and chronic oral exposure studies for MEK; and one to account for the absence of data for a second rodent specie for either MEK or 2-butanol. As is usual practice, the application of four full areas of uncertainty generally results in a total uncertainty factor of 3000, given the interrelationship among and overlap between the various areas of uncertainty described above.

MF -- None

I.A.4. ADDITIONAL STUDIES / COMMENTS (ORAL RfD)

Data on toxic effects in humans or laboratory animals following oral exposure to MEK are restricted to a limited number of acute studies. Oral LD50 values for MEK include 5522 and 2737 mg/kg in rats (Smyth et al., 1962 and Kimura et al., 1971, respectively) and 4,044 mg/kg in mice (Tanii et al., 1986). Single gavage doses of 15 mmol/kg MEK in corn oil (1082 mg/kg) produced no deaths or histological alterations in the livers of male Fischer 344 rats, but produced tubular necrosis in kidneys (Brown and Hewitt, 1984). Pre-administration of single gavage doses of MEK (or other ketonic solvents) enhanced the liver and kidney damage produced by a 0.5 mL/kg intraperitoneal dose of carbon tetrachloride (Brown and Hewitt, 1984). This MEK potentiation of carbon tetrachloride hepatotoxicity was also observed in similar experiments with male Sprague-Dawley rats (Dietz and Traiger, 1979).

At present there are insufficient oral exposure data of MEK from which to derive an oral RfD. Availability of oral exposure data of a metabolic intermediate of MEK, i.e., 2-butanol, was used to derive the RfD of MEK. The following is an explanation of the rationale for using the oral data of 2-butanol rather than attempting a route-to-route extrapolation of the available inhalation data for MEK.

Traiger and Bruckner (1976) have estimated that approximately 96% of an administered dose of 2-butanol is oxidized in vivo to MEK. The data from the Dietz et al. (1981) study support this estimation. Administration of 1776 mg/kg 2-butanol by gavage shows peak blood 2-butanol concentrations (0.59 mg/mL) within 2 hours; the compound is barely detectable after 16 hours. As the blood concentrations of 2-butanol fall, the peak concentrations of MEK (0.78 mg/mL) and 2,3-butanediol (0.21 mg/mL) occurred at 8 and 18 hours respectively. Ultimately, 2-butanol and MEK are metabolized through the same intermediates.

Additional metabolism of the ketone occurs by oxidation to hydroxylated intermediates such as 2,3-butanediol, all of which can be eliminated in the urine (DiVincenzo et al., 1977). DiVincenzo et al. (1976) have previously identified MEK, 2-butanol, and other oxidative metabolites of MEK in the serum of guinea pigs following administration of MEK.

A pharmacokinetic model was presented by Dietz et al. (1981) to describe the biotransformation of 2-butanol and MEK in rats when given a dose calculated to produce an equivalent calculated adjusted urinary concentration. When MEK is administered by gavage at a dose of 1690 mg/kg, the detection of the formation of 2-butanol and the oxidative metabolites corresponds to that previously reported in the guinea pig. By 18 hours post administration, MEK is barely detectable in the blood (peak concentration of 0.95 mg/mL at 4 hours), but a peak blood concentration (0.26 mg/mL) of the oxidative metabolite 2,3-butanediol can be detected. Peak blood concentrations of 2-butanol (0.033 mg/mL) occurred after 6 hours.

Although it is not known if the effects reported by Cox et al. (1975) are due to either 2-butanol directly or indirectly through another common metabolite, the weight of evidence of the available data argues for using the

butanol data as a surrogate approach to the development of the RfD for MEK. It is assumed in this surrogate approach that 2-butanol is not the active metabolite causing the effects reported by Cox, given the profile of metabolism for both 2-butanol and MEK. Therefore, it is appropriate to utilize data from the oral administration of 2-butanol in order to derive an RfD for MEK in lieu of appropriate oral data for MEK.

Decreased fetal body weight was also reported in pregnant mice exposed by inhalation to 0, 398, 1010, or 3020 ppm MEK (0, 1174, 2978, or 8906 mg/cu.m, respectively, assuming 25 C and 760 mm Hg) 7 hours/day during gestational days 6-15 (Schwetz et al., 1991; Mast et al., 1989). The only maternal effect observed was a concentration-related increase in relative liver and kidney weight. The difference was statistically significant in the dams exposed to 3020 ppm MEK. The biologic significance of this increase has not been ascertained. The decrease in fetal body weight was observed in the 3020-ppm group, however the difference was statistically significant only in the males. There was a statistically significant ($p<0.05$) trend with increasing concentration in the incidence of fetuses with misaligned sternebrae, but this trend was not apparent in the incidence of litters with misaligned sternebrae. Although increased incidence of fetuses and litters with malformations were observed in exposed groups compared with controls, the increases were not statistically significant. The observed fetal malformations (cleft palate, fused ribs, missing vertebrae and syndactyly) present in the exposed groups were not observed in concurrent or contemporary control groups of the same strain of mice. The Schwetz et al. (1991) study identified a NOAEL of 1126 ppm and a LOAEL of 3020 ppm for the occurrence of significant, developmental effects in mice including a decrease in fetal body weight, thereby corroborating the effects observed by Cox et al. (1975).

Sprague-Dawley rats were exposed to 0, 1126, or 2618 ppm MEK (0, 3320, or 7720 mg/cu.m, respectively, assuming 25 C and 760 mm Hg) 7 hours/day during gestational days 6-15 (Schwetz et al., 1974). The following endpoints were used to assess exposure-related effects: maternal (body weight, food intake, liver weight, SGOT levels, number of implantations/litter size) and fetal (examination for anomalies, incidence of fetal resorptions, fetal body measurements). No maternal effects or effect on the incidence of fetal resorptions were observed. A decrease in fetal body weight and crown-rump length were observed in the 1126 ppm offspring, however, these effects were not observed in the offspring of the rats exposed to 2618 ppm. There were no gross, soft tissue, or specific skeletal anomalies that occurred at a significantly increased incidence among litters of dams exposed to 1126 ppm MEK. However, the total number of litters containing fetuses with anomalous skeletons was significantly increased compared with controls. In the fetuses of the 2618-ppm group, there was a significantly increased number of fetuses and litters having gross anomalies (two acaudate fetuses with an imperforate anus and 2 brachygnathous fetuses). No single soft tissue anomaly occurred at a statistically significant increased incidence, but the total number of litters containing fetuses with soft tissue anomalies was significantly greater than in controls.

Groups of 25 pregnant Sprague-Dawley rats were exposed to 0, 412, 1002, or 3005 ppm MEK (0, 1215, 2956, or 8861 mg/cu.m, respectively, assuming 25 C and 760 mm Hg) 7 hours/day during gestational days 6-15 (Deacon et al., 1981). Decreased maternal body weight gain and increased water consumption were observed in the 3005 ppm group. No other maternal effects were noted. No

statistically significant differences in the incidence of external or soft-tissue alterations were observed among exposed fetuses. A significant decrease in the incidence of delayed ossification of interparietal bones of the skull and an increase in the incidence of extra lumbar ribs and in the occurrence of delayed ossification of cervical centra were noted at the 3005-ppm exposure level.

Data for humans and rats support the assumption that approximately 50% of inhaled MEK is absorbed. From measurements of environmental and exhaled air concentrations, Perbellini et al. (1984) calculated pulmonary retentions of about 70% in workers exposed to concentrations less than 300 ppm for 4 hours (most of the measurements were made at environmental concentrations at or below 100 ppm). From similar measurements, Liira et al. (1988) calculated a pulmonary retention of about 53% for male human volunteers exposed to 200 ppm for 4 hours. Kessler et al. (1988) reported a pulmonary retention of 40% for rats exposed to concentrations less than or equal to 180 ppm for up to about 14 hours.

Although a route-to-route extrapolation could be attempted from the inhalation data, a number of assumptions would need to be made with regard to the inhalation and oral absorption efficiencies making a route-to-route extrapolation limited at best. The developmental effects of MEK inhalation exposure are consistent with the developmental effects seen following oral exposure to 2-butanol and therefore make such an exercise plausible. However, the calculation of an inhalation absorption efficiency for MEK is problematic. The pulmonary retention values discussed above are calculated for exposures of 200 ppm (Liira et al., 1988) and 300 ppm (Perbellini et al., 1984) for a limited 4-hour exposure in humans. The pulmonary retention data of Kessler et al. (1988) using rats, although for a longer period of time (14 hours), was at a maximum concentration of 180 ppm. The calculation of the 40% pulmonary retention value is dependent upon a low concentration that is not limited by metabolic capacity but by transport to the metabolizing enzymes. This retention value, therefore, is valid only if related to normal physiologic processes. Inhalation effects of MEK are seen at concentrations an order of magnitude greater than was used to calculate the rat pulmonary retention value. The toxicity of MEK may be a result of challenges made to a saturable enzymatic detoxification mechanism. Therefore, it cannot be assumed that the pulmonary retention value will be the same at exposures of less than 180 ppm or at greater than 1800 ppm. For this reason, it is inappropriate to estimate the pulmonary retention value at these effect levels, thereby precluding derivation of an oral RfD based upon extrapolation from inhalation effects.

___I.A.5. CONFIDENCE IN THE ORAL RfD

Study -- Low
Data Base -- Low
RfD -- Low

Confidence in the principal study is low. The multigeneration/ developmental study for 2-butanol defined a critical effect that is corroborated by inhalation exposure data. Although the study employed an

adequate number of animals and examined appropriate endpoints, lowering the high-dose group from 3.0 to 2.0% confounded determination of the critical effect. Confidence in the data base is low. This RfD is based on a multigeneration developmental study for a compound that is nearly completely converted to MEK in a short period of time. This compound exhibits similar developmental effects as seen by inhalation exposure to MEK. However, the lack of oral data for MEK itself and the absence of data in a second specie precludes any higher level for data base confidence. This assessment for MEK is based upon the strength of data supporting the use of the 2-butanol multigeneration study and the concurrence of developmental effects for inhalation exposure to MEK and assumes that 2-butanol was not responsible for the fetal toxicity. There is a lack of data on the metabolism of 2-butanol and MEK over time thereby decreasing the confidence in the use of this surrogate approach. Therefore, confidence in the RfD is low.

___I.A.6. EPA DOCUMENTATION AND REVIEW OF THE ORAL RfD

Source Document -- This risk assessment is not presented in any existing U.S. EPA document.

Other EPA Documentation -- U.S. EPA, 1984, 1985

Agency Work Group Review -- 06/24/1985, 07/08/1985, 05/16/1990, 07/17/1991, 09/23/1992,
11/05/1992

Verification Date -- 11/05/1992

___I.A.7. EPA CONTACTS (ORAL RfD)

Please contact the Risk Information Hotline for all questions concerning this assessment or IRIS, in general, at (513)569-7254 (phone), (513)569-7159 (FAX) or RIH.IRIS@EPAMAIL.EPA.GOV (internet address).

__I.B. REFERENCE CONCENTRATION FOR CHRONIC INHALATION EXPOSURE (RfC)

Substance Name -- Methyl ethyl ketone (MEK)

CASRN -- 78-93-3
Last Revised -- 07/01/1992

The inhalation Reference Concentration (RfC) is analogous to the oral RfD and is likewise based on the assumption that thresholds exist for certain toxic effects such as cellular necrosis. The inhalation RfC considers toxic effects for both the respiratory system (portal-of-entry) and for effects peripheral to the respiratory system (extrarespiratory effects). It is expressed in units of mg/cu.m. In general, the RfC is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily inhalation exposure of the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. Inhalation RfCs were derived according to the Interim Methods for Development of Inhalation Reference Doses (EPA/600/8-88/066F August 1989) and subsequently, according to Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry (EPA/600/8-90/066F October 1994). RfCs can also be derived for the noncarcinogenic health effects of substances that are carcinogens. Therefore, it is essential to refer to other sources of information concerning the carcinogenicity of this substance. If the U.S. EPA has evaluated this substance for potential human carcinogenicity, a summary of that evaluation will be contained in Section II of this file.

___I.B.1. INHALATION RfC SUMMARY

Critical Effect	Exposures*	UF	MF	RfC
Decreased fetal birth weight Mouse Developmental Study Schwetz et al., 1991; Mast et al., 1989	NOAEL: 2978 mg/cu.m (1010 ppm, nominal) NOAEL(ADJ): 2978 mg/cu.m NOAEL(HEC): 2978 mg/cu.m LOAEL: 8906 mg/cu.m (3020 ppm, nominal) LOAEL(ADJ): 8906 mg/cu.m LOAEL(HEC): 8906 mg/cu.m	1000	3	1E+0 mg/cu.m

*Conversion Factors: MW = 72.1 Assuming 25 C and 760 mm Hg. NOAEL (mg/cu.m) = 1010 ppm x 72.1/24.45 = 2978 mg/cu.m. Currently, the approach for dose-response analysis of developmental endpoints does not duration-adjust exposure concentrations. NOAEL(ADJ) = NOAEL = 2978 mg/cu.m. The NOAEL(HEC) was calculated for a gas:extrarespiratory effect assuming periodicity was attained. Since the b:a lambda values are unknown for the experimental animal species (a) and human (h), a default value of 1.0 is used for this ratio. NOAEL(HEC) = NOAEL(ADJ) x (b:a lambda(a)/b:a lambda(h)) = 2978 mg/cu.m.

___I.B.2. PRINCIPAL AND SUPPORTING STUDIES (INHALATION RfC)

Schwetz, B.A., T.J. Mast, R.J. Weigel, J.A. Dill and R.E. Morrissey. 1991. Developmental toxicity of inhaled methyl ethyl ketone in mice. Fund. Appl. Toxicol. 16: 742-748.

Mast, T.J., J.A. Dill, J.J. Evanoff, R.L. Rommereim, R.J. Weigel and R.B. Westerberg. 1989. Inhalation developmental toxicology studies: Teratology study of methyl ethyl ketone in mice. Final Report. Prepared by Pacific Northwest Laboratory, Battelle Memorial Institute, for the National Toxicology Program, Washington, DC. PNL-6833 UC-408.

Pregnant Swiss mice were exposed to 0, 398, 1010 or 3020 ppm methyl ethyl ketone (0, 1174, 2978 or 8906 mg/cu.m, respectively, assuming 25 C and 760 mm Hg) 7 hours/day during gestational days 6-15. The Schwetz et al. (1991) and the Mast et al. (1989) reports are the same developmental mouse study presented in different formats and are hence considered as one single study. The number of dams exposed to methyl ethyl ketone ranged from 23-28 mice depending upon exposure group. The dams were killed on gestational day 18. The only maternal effect observed was a concentration-related increase in relative liver and kidney weight. The difference was statistically significant only in the dams exposed to 3020 ppm methyl ethyl ketone. The biological significance of this increase has not been ascertained. A decrease in fetal body weight was also observed in the 3020 ppm exposed group; however, the difference was significant only in the males. There was a significant ($p<0.05$) trend in the incidence of misaligned sternebrae present in fetuses but not reflected in a similar analysis of litters of the animals exposed to 3020 ppm. Additionally, although no significant increase of any single malformation was found, there were several malformations (cleft palate, fused ribs, missing vertebrae and syndactyly) present at low incidences in exposed groups.

Neither maternal nor developmental toxicity was observed at exposures at or less than 1010 ppm (2978 mg/cu.m). At 3020 ppm (8906 mg/cu.m), an equivocal maternal effect was reported; however, mild developmental effects (decreased fetal body weight and misaligned sternebrae) were found. Based on the absence of both maternal and developmental toxic effects, a NOAEL of 1126 ppm (HEC=2978 mg/cu.m) is established. The LOAEL is established at 3020 ppm (HEC=8906 mg/cu.m) based on the appearance of mild, but significant developmental effects.

Groups of 21-23 pregnant Sprague-Dawley rats were exposed to 0, 1126 or 2618 ppm methyl ethyl ketone (0, 3320 or 7720 mg/cu.m, respectively, assuming 25 C and 760 mm Hg) 7 hours/day during gestational days 6-15 (Schwetz et al., 1974). The following endpoints were used to assess exposure-related effects: maternal body weight, food intake, liver weight, SGOT levels, and number of implantations/litter size; and fetal anomalies, incidence of resorptions, and fetal body measurements.

No maternal effects or effects on the incidence of fetal resorptions were observed. A decrease in fetal body weight and crown-to-rump length was observed in the offspring exposed to 1126 ppm; however, these effects were not observed in the offspring of the rats exposed to 2618 ppm There were no gross, soft tissue or specific skeletal anomalies that occurred at a significantly increased incidence among litters of dams exposed to 1126 ppm methyl ethyl ketone. However, the total number of litters containing fetuses

with anomalous skeletons was increased significantly compared to controls. In the fetuses exposed to 2618 ppm methyl ethyl ketone, there was a significantly increased number of fetuses and litters having gross anomalies (two acaudate fetuses with an imperforate anus and two brachygnathous fetuses) compared to the incidence among controls. No single soft tissue anomaly occurred at a statistically significant increased incidence, but the total number of litters containing fetuses with soft tissue anomalies was significantly greater than in controls.

The study by Deacon et al. (1981) was conducted to determine the repeatability of the fetotoxic effects observed in the Schwetz et al. (1974) study. Groups of 25 pregnant Sprague-Dawley rats were exposed to 0, 412, 1002 or 3005 ppm methyl ethyl ketone (0, 1215, 2955 or 8861 mg/cu.m, respectively, assuming 25 C and 760 mm Hg) 7 hours/day during gestational days 6-15. Decreased maternal body weight gain and increased water consumption were observed in the group exposed to 3005 ppm. No other maternal effects were noted. No statistically significant differences in the incidence of external or soft-tissue alterations were observed among exposed fetuses. A significant decrease in the incidence of delayed ossification of interparietal bones of the skull and an increase in the incidence of extra lumbar ribs and in the occurrence of delayed ossification of cervical centra were noted at the 3005 ppm exposure level.

___I.B.3. UNCERTAINTY AND MODIFYING FACTORS (INHALATION RfC)

UF -- An uncertainty factor of 1000 reflects factors of 10 to account for interspecies extrapolation, sensitive individuals, and incomplete data base including a lack of chronic and reproductive toxicity studies.

MF -- A modifying factor of 3 was used to address the lack of unequivocal data for respiratory tract (portal-of-entry) effects.

___I.B.4. ADDITIONAL STUDIES/COMMENTS (INHALATION RfC)

Slight nose and throat irritation was observed in 10 human volunteers exposed to 100 ppm methyl ethyl ketone (HEC=295 mg/cu.m) for 5 minutes. Exposure to 300 ppm (HEC=885 mg/cu.m) was judged to be intolerable by the subjects (Nelson et al., 1943).

Male and female volunteers (12-13/sex) were exposed to 186 ppm (HEC=549 mg/cu.m, assuming 25 C and 760 mm Hg) for 4 hours. No statistically significant changes in neurobehavioral performance were observed (Dick et al., 1988).

Groups of male and female Fischer 344 rats (n=15) were exposed to 0, 1254, 2518 or 5041 ppm methyl ethyl ketone (0, 3698, 7425 or 14,865 mg/cu.m,

respectively, assuming 25 C and 760 mm Hg) 6 hours/day, 5 days/week for 90 days (Cavender et al., 1983; Toxigenics, 1981). For each exposure group, 10 animals were used for general histopathology and 5 animals for neuropathologic examination. Tissues examined included nasal cavity, trachea and bronchi, lung, liver and kidney. The prevalence of chronic respiratory disease in the pulmonary region was 100% across control and all exposure groups. There were also high prevalences of nasal inflammation, including submucosal lymphocytic infiltration and lumenal exudate, across control and all exposure groups. These latter lesions, however, varied slightly across the nasal cavity section examined and with exposure level tested. Although the authors suggest that the pulmonary lesions are secondary to mycoplasma infection, no infectious agent was cultured. In other investigations utilizing a model for Mycoplasma pulmonis, pulmonary lesions showed a concentration-response indicative of upper airway irritation (Broderson et al., 1976). The high prevalences of both the nasal and pulmonary lesions in this study preclude unequivocal interpretation regarding respiratory effects. No histopathologic alterations of other major tissues or of neuropathology were observed. An increase in absolute and relative liver weight and relative kidney weight was observed in the animals of both sexes exposed to 5041 ppm. An increase in serum alkaline phosphatase levels was also observed in the female rats exposed to 5041 ppm methyl ethyl ketone. At the highest concentration, females were found to have decreased absolute and increased relative brain weight, however, no pathological changes were observed in the medulla oblongata or the sciatic and tibial nerves. No functional tests (pulmonary or neurologic) were performed in these studies. Based on toxicity remote to the respiratory tract described above, this study provisionally identifies a NOAEL of 2518 ppm (HEC=1326 mg/cu.m) and a LOAEL of 5041 ppm (HEC=2654 mg/cu.m).

Groups of 5 male Wistar rats were exposed to 10,000 ppm methyl ethyl ketone (29,489 mg/cu.m, assuming 25 C and 760 mm Hg) 8 hours/day, 7 days/week for 15 weeks. Because of severe upper respiratory tract irritation, the concentration was lowered to 6000 ppm (17,693 mg/cu.m). The exposed rats died after 7 weeks of exposure; the cause of death was bronchopneumonia. Severe hindlimb weakness was observed in all animals given a methyl ethyl ketone/n-hexane mixture by the 9th week of exposure, which progressed to severe paresis. These effects were observed again when the experiment was repeated. However, these effects were not observed when methyl ethyl ketone was administered alone (Altenkirch et al., 1978).

A group of 25 adult rats (strain not given) was exposed to 235 ppm (693 mg/cu.m) 7 hours/day, 5 days/week for 12 weeks (LaBelle and Brieger, 1955). The dose duration-adjusted concentration is equivalent to 144 mg/cu.m. A control group was included, but the number of animals was not given. At the end of the study, 15 rats were examined microscopically (organs not given) and hematologically (hemoglobin, erythrocyte, leukocyte, neutrophil, lymphocyte, and monocyte counts). The remaining 10 rats were reserved for growth studies. No adverse effects were observed, but only a few critical parameters were measured for a single exposure concentration. Similarly, 15 guinea pigs were exposed to methyl ethyl ketone at the same concentration as were the rats. No adverse effects were reported for the exposed guinea pigs. However, this information is only presented qualitatively in the report. Furthermore, it was reported that the guinea pigs experienced a vitamin deficiency possibly contributing to two deaths during the exposure period.

Male Wistar rats (8/group) were exposed to 0 or 200 ppm methyl ethyl

ketone (0 or 590 mg/cu.m, assuming 25 C and 760 mm Hg) 12 hours/day, 7 days/week for 24 weeks. A slight increase in motor nerve conduction velocity and mixed nerve conduction velocity and a decrease in distal motor latency were observed at 4 weeks of exposure. However, no difference was observed after 4 weeks [NOEL(HEC)=295 mg/cu.m] (Takeuchi et al., 1983).

Groups of 12 Sprague-Dawley rats were continuously exposed to 1125 ppm methyl ethyl ketone (3318 mg/cu.m, assuming 25 C and 760 mm Hg) for 16-55 days. Pathological examination of the sciatic nerve and intrinsic foot muscles revealed no peripheral neuropathy [NOEL(HEC)=3318 mg/cu.m] (Saida et al., 1976).

Four baboons were exposed to 100 ppm methyl ethyl ketone (295 mg/cu.m, assuming 25 C and 760 mm Hg) continuously for 7 days. Operant conditioning behavior conducted during exposure was compared to pre-exposure test scores. The operant behavior selected was a match-to-sample discrimination task and the experimental protocol allowed the performance of each baboon during exposure to be compared to his performances during a clean air exposure in the same chamber immediately prior to each exposure. There was no significant effect on accuracy; however, there was a decrease in mean response time and response during delay (Geller et al., 1979). The authors (Geller et al., 1979) suggested that this could be an early manifestation of the incoordination and narcosis observed in guinea pigs after acute exposure to 10,000 ppm methyl ethyl ketone (29,489 mg/cu.m, assuming 25 C and 760 mm Hg) (Patty et al., 1935). However, it should be pointed out that each baboon in this study was exposed to four different chemicals of which methyl ethyl ketone was given second.

Swiss mice were exposed to various levels of methyl ethyl ketone. A decrease in the immobility developed in a behavioral despair swimming test was observed. A 50% decrease in immobility (ID50) was observed at 2065 ppm (6089 mg/cu.m, assuming 25 C and 760 mm Hg) (DeCeaurriz et al., 1983).

Although the role of methyl ethyl ketone in potentiating peripheral neuropathies caused by potent neurotoxins such as hexane and methyl n-butylketone is documented (Altenkirch et al., 1978; Saida et al., 1976), current experimental data indicate that, by itself, methyl ethyl ketone has little if any neurotoxic potential. Several studies examining neurotoxicity of methyl ethyl ketone have employed neurohistopathology to evaluate toxicity. No peripheral neurohistopathological changes were noted in rats exposed continuously to 1125 ppm methyl ethyl ketone for up to 5 months (Saida et al., 1976). No treatment-related central or peripheral neurohistopathology was observed in rats exposed for 90 days (6 hours/day, 5 days/week) to methyl ethyl ketone concentrations up to 5041 ppm (Toxigenics, 1981; also reported in Cavender et al., 1983). In a study combining experiments of methyl ethyl ketone and n-hexane, Altenkirch et al. (1978) reported that all 10 male rats exposed to 6000 ppm methyl ethyl ketone (8 hours/day, 7 days/week) died in the 7th week without neurological symptoms or pathology although central and extensive peripheral neurohistopathology was observed in animals concurrently exposed to n-hexane. The authors also reported that animals in all exposure groups (both methyl ethyl ketone and hexane) were somnolent during exposure. A few studies have attempted to examine neurological deficits through functional testing in addition to histopathology. Takeuchi et al. (1983) reported an alteration in nerve conduction velocities but only in the 4th week of a 24-week exposure to 200 ppm methyl ethyl ketone; the alteration was not

corroborated by histopathology and was in the opposite direction to that predicted by peripheral neurotoxins such as n-hexane. Results from other functional-deficit studies in humans (Dick et al., 1988) have been negative and in baboons (Geller et al., 1979), inconclusive, perhaps due to experimental design problems. At present, there is no convincing experimental evidence that methyl ethyl ketone, by itself, is neurotoxic to either experimental animals or humans other than possibly inducing CNS depression at high exposure levels.

___I.B.5. CONFIDENCE IN THE INHALATION RfC

Study -- Medium
Data Base -- Low
RfC -- Low

Confidence in the principal study is medium. This and other developmental studies were well-designed and tested several exposure concentrations and several endpoints of toxicity. Although the principal and supporting studies corroborate an effect level for developmental toxicity endpoints, there are insufficient data presented for possible respiratory effects. Confidence in the data base is low. There are no multigenerational studies and only one subchronic study. Furthermore, these studies do not adequately address portal-of-entry effects given that short-term exposure to higher concentrations than that established for the LOAEL cause nasal and throat irritation in both human and experimental animal species. Reflecting medium confidence in the principal study and low confidence in the data base, confidence in the RfC is low.

___I.B.6. EPA DOCUMENTATION AND REVIEW OF THE INHALATION RfC

Source Document -- This is not presented in any existing U.S. EPA document

Other EPA Documentation -- None

Agency Work Group Review -- 04/21/1988, 05/26/1988, 03/22/1990, 05/16/1990, 07/17/1991

Verification Date -- 07/17/1991

___I.B.7. EPA CONTACTS (INHALATION RfC)

Please contact the Risk Information Hotline for all questions concerning this

assessment or IRIS, in general, at (513)569-7254 (phone), (513)569-7159 (FAX) or RIH.IRIS@EPAMAIL.EPA.GOV (internet address).

_II. CARCINOGENICITY ASSESSMENT FOR LIFETIME EXPOSURE

Substance Name -- Methyl ethyl ketone (MEK)
CASRN -- 78-93-3
Last Revised -- 12/01/1989

Section II provides information on three aspects of the carcinogenic assessment for the substance in question; the weight-of-evidence judgment of the likelihood that the substance is a human carcinogen, and quantitative estimates of risk from oral exposure and from inhalation exposure. The quantitative risk estimates are presented in three ways. The slope factor is the result of application of a low-dose extrapolation procedure and is presented as the risk per (mg/kg)/day. The unit risk is the quantitative estimate in terms of either risk per ug/L drinking water or risk per ug/cu.m air breathed. The third form in which risk is presented is a drinking water or air concentration providing cancer risks of 1 in 10,000, 1 in 100,000 or 1 in 1,000,000. The rationale and methods used to develop the carcinogenicity information in IRIS are described in The Risk Assessment Guidelines of 1986 (EPA/600/8-87/045) and in the IRIS Background Document. IRIS summaries developed since the publication of EPA's more recent Proposed Guidelines for Carcinogen Risk Assessment also utilize those Guidelines where indicated (Federal Register 61(79):17960-18011, April 23, 1996). Users are referred to Section I of this IRIS file for information on long-term toxic effects other than carcinogenicity.

__II.A. EVIDENCE FOR CLASSIFICATION AS TO HUMAN CARCINOGENICITY

___II.A.1. WEIGHT-OF-EVIDENCE CLASSIFICATION

Classification -- D; not classifiable as to human carcinogenicity

Basis -- Based on no human carcinogenicity data and inadequate animal data.

II.A.2. HUMAN CARCINOGENICITY DATA

None.

II.A.3. ANIMAL CARCINOGENICITY DATA

Inadequate. No data were available to assess the carcinogenic potential of methyl ethyl ketone by the oral or inhalation routes. In a skin carcinogenesis study, two groups of 10 male C3H/He mice received dermal applications of 50 mg of a solution containing 25 or 29% methyl ethyl ketone in 70% dodecylbenzene twice a week for 1 year. No skin tumors developed in the group of mice treated with 25% methyl ethyl ketone. After 27 weeks, a single skin tumor developed in 1 of 10 mice receiving 29% methyl ethyl ketone (Horton et al., 1965).

II.A.4. SUPPORTING DATA FOR CARCINOGENICITY

Methyl ethyl ketone was not mutagenic for Salmonella typhimurium strains TA98, TA100, TA1535, or TA1537 with or without rat hepatic homogenates (Florin et al., 1980; Douglas et al., 1980). Methyl ethyl ketone induced aneuploidy in the diploid D61, M strain of Saccharomyces cerevisiae (Zimmermann et al., 1985). Low levels of methyl ethyl ketone combined with low levels of nocodazole (another inducer of aneuploidy), also produced significantly elevated levels of aneuploidy in the system (Mayer and Goin, 1987).

II.B. QUANTITATIVE ESTIMATE OF CARCINOGENIC RISK FROM ORAL EXPOSURE

None.

II.C. QUANTITATIVE ESTIMATE OF CARCINOGENIC RISK FROM INHALATION EXPOSURE

None.

__II.D. EPA DOCUMENTATION, REVIEW, AND CONTACTS (CARCINOGENICITY ASSESSMENT)

___II.D.1. EPA DOCUMENTATION

U.S. EPA. 1985. Health and Environmental Effects Profile for Methyl Ethyl Ketone. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste and Emergency Response, Washington, DC.

U.S. EPA. 1988. Updated Health Effects Assessment for Methyl Ethyl Ketone. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste and Emergency Response, Washington, DC.

The 1988 Updated Health Effects Assessment for Methyl Ethyl Ketone has received Agency review.

___II.D.2. REVIEW (CARCINOGENICITY ASSESSMENT)

Agency Work Group Review -- 05/30/1989

Verification Date -- 05/30/1989

___II.D.3. U.S. EPA CONTACTS (CARCINOGENICITY ASSESSMENT)

Please contact the Risk Information Hotline for all questions concerning this assessment or IRIS, in general, at (513)569-7254 (phone), (513)569-7159 (FAX) or RIH.IRIS@EPAMAIL.EPA.GOV (internet address).

_VI. BIBLIOGRAPHY

Substance Name -- Methyl ethyl ketone (MEK)
CASRN -- 78-93-3
Last Revised -- 06/01/1993

__VI.A. ORAL RfD REFERENCES

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_VII. REVISION HISTORY

Substance Name -- Methyl ethyl ketone (MEK)
CASRN -- 78-93-3

Date	Section	Description
03/31/1987	I.A.6.	Documentation corrected
03/01/1988	I.A.2.	Paragraph 2 clarified
07/01/1989	II.	Carcinogen assessment now under review
07/01/1989	VI.	Bibliography on-line
12/01/1989	II.	Carcinogen assessment on-line
12/01/1989	VI.C.	Carcinogen references added
04/01/1990	I.B.	Inhalation RfC now under review
06/01/1990	I.A.	Oral RfD summary noted as pending change
06/01/1990	IV.F.1.	EPA contact changed
08/01/1991	I.A.	Withdrawn pending further review
08/01/1991	VI.A.	Oral RfD references withdrawn
01/01/1992	IV.	Regulatory Action section on-line
07/01/1992	I.B.	Inhalation RfC on-line
07/01/1992	VI.B.	Inhalation RfC references on-line
08/01/1992	VI.B.	Inhalation RfC references clarified
10/01/1992	I.A.	Work group review date added
12/01/1992	I.A.	Work group review date added
05/01/1993	I.A.	Oral RfD summary replaced; RfD changed
05/01/1993	VI.A.	Oral RfD references replaced
06/01/1993	VI.C.	Minor correction
04/01/1997	III.,IV., V.	Drinking Water Health Advisories, EPA Regulatory Actions, and Supplementary Data were removed from IRIS on or before April 1997. IRIS users were directed to the appropriate EPA Program Offices for this information.

VIII. SYNONYMS

Substance Name -- Methyl ethyl ketone (MEK)
CASRN -- 78-93-3
Last Revised -- 01/31/1987

78-93-3
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OPPT Chemical Fact Sheet EPA 749-F-94-015

CHEMICALS IN THE ENVIRONMENT: METHYL ETHYL KETONE (CAS NO. 78-93-3)

prepared by
OFFICE OF POLLUTION PREVENTION AND TOXICS
U.S. ENVIRONMENTAL PROTECTION AGENCY
September 1994

Chemicals can be released to the environment as a result of their manufacture, processing, and use. EPA has developed information summaries on selected chemicals to describe how you might be exposed to these chemicals, how exposure to them might affect you and the environment, what happens to them in the environment, who regulates them, and whom to contact for additional information. EPA is committed to reducing environmental releases of chemicals through source reduction and other practices that reduce creation of pollutants.

WHAT IS METHYL ETHYL KETONE, HOW IS IT USED, AND HOW MIGHT I BE EXPOSED?

Methyl ethyl ketone (also called MEK and 2-butanone) is a colorless, flammable liquid. It occurs naturally in certain foods and beverages. It is produced in large amounts (estimated to be 500 million pounds in 1992) by three companies in the United States. US demand for MEK is likely to decrease gradually until makers of protective surface coatings begin using other substances. Once companies make this change, US demand for MEK is likely to fall more rapidly. The largest users of MEK are companies that add it to protective surface coatings. Other companies add MEK to adhesives, printing inks, paint removers, and special lubricating oils. Companies also use MEK to make other chemicals, including those used as drugs and cosmetics. Small amounts of MEK are used to sterilize surgical instruments, hypodermic needles, syringes, and dental instruments. It is also used to extract vegetable oil.

Exposure to MEK can occur in the workplace or in the environment following releases to air, water, land, or groundwater. Exposure can also occur when people use certain paints, paint removers, or adhesives. Methyl ethyl ketone enters the body when breathed in with contaminated air or when consumed with contaminated food or water. It can also be absorbed through skin contact. It is not likely to remain in the body due to its breakdown and removal in expired air and in urine.

WHAT HAPPENS TO METHYL ETHYL KETONE IN THE ENVIRONMENT?

Methyl ethyl ketone evaporates when exposed to air. It dissolves when mixed with water. Most direct releases of MEK to the environment are to air. It can also evaporate from water and soil exposed to air. Once in air, it is expected to break down to other chemicals. Microorganisms that live in water and in soil can also break down MEK. Because it is a liquid that does not bind well to soil, MEK that makes its way into ground can move through the ground and enter groundwater. Plants and animals are not likely to store methyl ethyl ketone.

HOW DOES METHYL ETHYL KETONE AFFECT HUMAN HEALTH AND THE ENVIRONMENT?

Effects of methyl ethyl ketone on human health and the environment depend on how much MEK is present and the length and frequency of

exposure. Effects also depend on the health of a person or the condition of the environment when exposure occurs.

Breathing MEK for short periods of time, such as when painting in a poorly vented area, can adversely affect the nervous system. Effects range from headaches, dizziness, nausea, and numbness in fingers and toes to unconsciousness. MEK vapor irritates the eyes, the nose, and the throat. Direct, prolonged contact with liquid methyl ethyl ketone irritates the skin and damages the eyes. These effects are not expected to occur at levels of MEK that are normally found in the environment.

Human health effects associated with breathing or otherwise consuming smaller amounts of methyl ethyl ketone over long periods of time are not known. Workers have developed dermatitis, upset stomachs, loss of appetite, headaches, dizziness, and weakness as a result of repeated exposure to MEK. Laboratory studies show that exposure to large amounts of MEK in air causes animals to give birth to smaller offspring. Studies also show that repeat exposure to large amounts of MEK in air causes adverse liver and kidney effects in animals.

Methyl ethyl ketone by itself is not likely to cause environmental harm at levels normally found in the environment. MEK can contribute to the formation of photochemical smog when it reacts with other volatile organic carbon substances in air.

WHAT EPA PROGRAM OFFICES REGULATE METHYL ETHYL KETONE, AND UNDER WHAT LAWS IS IT REGULATED?

EPA OFFICE	LAW	PHONE NUMBER
Pollution Prevention & Toxics	Toxic Substances Control Act	(202) 554-1404
	Emergency Planning and Community Right-to-Know Act (EPCRA) Regulations (Sec. 313)	(800) 535-0202
	Toxics Release Inventory data	(202) 260-1531
Air	Clean Air Act	(919) 541-0888
Solid Waste & Emergency Response	Comprehensive Environmental Response, Compensation, and Liability Act (Superfund)/ Resource Conservation and Recovery Act / EPCRA (Sec. 304/311/312)	(800) 535-0202
Water	Safe Drinking Water Act	(800) 426-4791

A technical support document can be requested from the TSCA Assistance Information Service, (202) 554-1404.

WHAT OTHER FEDERAL AGENCIES OR GROUPS CAN I CONTACT FOR INFORMATION ON METHYL ETHYL KETONE?

AGENCY/GROUP	PHONE NUMBER
Agency for Toxic Substances and Disease Registry	(404) 639-6000
American Conference of Governmental Industrial Hygienists	(513) 742-2020
Consumer Product Safety Commission	(301) 504-0994
Food and Drug Administration	(301) 443-3170
National Institute for Environmental Health Sciences (EnviroHealth Clearinghouse)	(800) 643-4794
National Institute for Occupational Safety and Health (NIOSH)	(800) 356-4674

Occupational Safety and Health Administration
(Check your local phone book under U.S. Department of Labor)

EPA 749-F-94-015a

CHEMICAL SUMMARY FOR METHYL ETHYL KETONE

prepared by
OFFICE OF POLLUTION PREVENTION AND TOXICS
U.S. ENVIRONMENTAL PROTECTION AGENCY
September 1994

This summary is based on information retrieved from a systematic search limited to secondary sources (see Appendix A). These sources include online databases, unpublished EPA information, government publications, review documents, and standard reference materials. No attempt has been made to verify information in these databases and secondary sources.

I. CHEMICAL IDENTITY AND PHYSICAL/CHEMICAL PROPERTIES

The chemical identity and physical/chemical properties of methyl ethyl ketone are summarized in Table 1.

TABLE 1. CHEMICAL IDENTITY AND CHEMICAL/PHYSICAL PROPERTIES OF METHYL ETHYL KETONE

Characteristic/Property	Data	Reference
CAS No.	78-93-3	
Common Synonyms	2-Butanone, MEK	Verschueren 1983
Molecular Formula	C4H80	
Chemical Structure	O || CH3-C-CH2-CH3	
Physical State	liquid	Budavari 1989
Molecular Weight	72.10	Budavari 1989
Melting Point	-86øC	Budavari 1989
Boiling Point	79.6øC	Budavari 1989
Water Solubility	353 g/L @ 10øC; 190 g/L @ 90øC	Verschueren 1983
Specific gravity	0.805 @ 20/4øC	Verschueren 1983
Vapor Density (air = 1)	2.41	Verschueren 1983
KOC	4.5 -50 (estimated)	U.S. EPA 1989
Log KOW	0.29 (estimated)	U.S. EPA 1989
Vapor Pressure	77.5 mm Hg @ 20øC 98.0 mm Hg @ 25øC	Verschueren 1983 U.S. EPA 1985
Reactivity	Liquid and vapor are flammable.	U.S. Air Force 1989
Flash Point	-6øC (closed cup)	Budavari 1989
Henry's Law Constant	4.16 to 6.11 X 10-5 atm-m3/mol @ 25øC (estimated)	U.S. EPA 1985
Fish Bioconcentration Factor	<1 (estimated)	U.S. EPA 1985
Odor Threshold	5 to 10 ppm (in air)	U.S. Air Force 1989
Conversion Factors	1 ppm = 2.94 mg/m3 1 mg/m3 = 0.34 ppm	Verschueren 1983

II. PRODUCTION, USE, AND TRENDS

A. Production

There are three methyl ethyl ketone producers in the United States. Table 2 lists producers, plant locations, and plant capacities. Annual US capacity is approximately 545 million pounds. In 1992, an estimated 494 million pounds of methyl ethyl ketone were produced in the US. During that same year, 55 million pounds were imported into the US and 112 million pounds were exported (Mannsville 1993).

B. Use

Methyl ethyl ketone is used in a number of industrial applications.

The primary use of methyl ethyl ketone, accounting for approximately 63 percent of all use, is as a solvent in protective coatings. It is also used as a solvent in adhesives; printing inks; paint removers; in the production of magnetic tapes; and in dewaxing lubricating oil. Methyl ethyl ketone is used as a chemical intermediate in several reactions, including condensation; halogenation; ammonolysis; and oxidation. Small amounts of methyl ethyl ketone are also used as a sterilizer for surgical instruments, hypodermic needles, syringes, and dental instruments; as an extraction solvent for hardwood pulping and vegetable oil; and as a solvent in pharmaceutical and cosmetic production (Mannsville 1993; HSDB 1994). Table 3 shows the estimated 1992 US end-use pattern for methyl ethyl ketone.

C. Trends

Demand for methyl ethyl ketone is expected to decrease gradually until alternative, low volatile organic carbon (VOC) coating technologies are readily available (Mannsville 1993). Once such alternatives are available, demand is expected to decrease more rapidly.

TABLE 2. United States Producers of Methyl Ethyl Ketone

Company	Plant Location	Plant Capacity (in millions of pounds)
Exxon Chemical	Baton Rouge, LA	230
Hoechst Celanese	Pampa, TX	85
Shell Chemical	Norco, LA	230

Source: Mannsville 1993.

TABLE 3. Estimated 1992 United States End-Use Pattern of Methyl Ethyl Keton

Use of Methyl Ethyl Ketone (typical Standard Industrial Classification (SIC) Code) (see end note 1)	Percentage of US Methyl Ethyl Ketone Use
Protective coatings solvent	

(production, SIC 2851)	63%
Adhesives solvent (production, SIC 2891)	13%
Magnetic tapes (production, SIC 3652, 3695)	10%
Lubricating oil dewaxing (production, SIC 2992)	5%
Chemical intermediate (production, SIC 2865, 2869)	4%
Printing inks (production, SIC 2893)	3%
Miscellaneous (no applicable SIC Code(s))	2%

Source: Mannsville 1993.

III. ENVIRONMENTAL FATE

A. Environmental Release

Of the total methyl ethyl ketone released to the environment almost all eventually enters the air. Methyl ethyl ketone is released into the environment from industrial and domestic uses. The largest man made sources of methyl ethyl ketone release are from its primary use as a solvent for coatings, resins, and adhesives (U.S. EPA 1985). Methyl ethyl ketone has been found in cigarette smoke (500 ppm) and in gasoline engine exhaust (<0.1-1.0 ppm) (Verschueren 1983). Its use as a solvent in polyvinyl chloride pipe joint cement has introduced the chemical into drinking water (4.5 ppm, 6 months after installation) (HSDB 1994). It occurs naturally and has been found in a number of foods and beverages including swiss cheese (0.3 ppm), cream (0.154-0.177 ppm), barley, bread, honey, oranges, black tea, rum, non-alcoholic beverages (70 ppm), and ice cream (270 ppm) (HSDB 1994).

In 1992, releases of methyl ethyl ketone to environmental media, as reported to the Toxic Chemical Release Inventory by certain types of US industries totaled about 91.3 million pounds. Of this amount, a total of 90.5 million pounds (99%) was released to the atmosphere, 153 thousand pounds were released to surface water, 365 thousand pounds to underground injection, and 242 thousand pounds were released to land (TRI92 1994).

Although the atmospheric concentration of methyl ethyl ketone increases during episodes of severe photochemical smog (up to 14 ppb in Los Angeles, CA during a photochemical pollution episode), ambient concentrations are usually below the detection limit (0.01 ppb) in most urban areas. Air levels averaging 64 ppb have been measured near industrial sources of the chemical, and a concentration of 94 ppm has been measured in the vicinity of a chemical reclamation plant (HSDB 1994). Methyl ethyl ketone was detected in less than 5% of groundwater samples in a federal survey of drinking water supplies, and in only one (found at a level of 23 ppb) of 204 sites from 14 heavily industrialized river basins in the United States. The chemical has been detected in clouds, fog, and ice fog in California (trace-0.47 ppm in positive samples), but not detected in rain. It was found in rain in Japan. It was also detected in the trench leachate from two low-level radioactive disposal sites (HSDB 1994).

B. Transport

Methyl ethyl ketone is not expected to be retarded by adsorption to soils rich in organic material [estimated Koc = 4.5-50 (U.S. EPA 1989)]; therefore, it is expected to be mobile in soil and,

subject to leaching from landfills. The relatively high vapor pressure [98.0 mm Hg @ 25øC (U.S. EPA 1985)] and estimated Henry's Law constant (4.16-6.11 x 10-5 atm m3/mol @ 25øC) indicate that it can volatilize from moist and dry soil (HSDB 1994). It does not adsorb significantly to suspended solids, and will volatilize to the atmosphere from surface waters (HSDB 1994; U.S. EPA 1985).

C. Transformation/Persistence

1. Air - The main degradation pathway for methyl ethyl ketone in the atmosphere is reaction with photochemically produced hydroxyl radicals, primarily producing acetaldehyde. The half-life of methyl ethyl ketone from the reaction with hydroxyl radicals has been estimated to be about 2.3 days (HSDB 1994). Direct photolysis with a calculated half-life of about 15.4 hours at a solar zenith angle of 30ø is expected to occur (U.S. EPA 1985). Deposition by rain or fog may play a minor role in transporting methyl ethyl ketone from the atmosphere. It has also been shown to be reactive in smog chamber studies (U.S. EPA 1985).

2. Soil - In wet or dry soil, methyl ethyl ketone will volatilize to air and may undergo photolysis on the soil surface (U.S. EPA 1985). It is also highly mobile and may be leached from the soil by water, and has been shown to be degradated by cultures of soil bacteria (U.S. EPA 1985).

3. Water - The most important fate process for methyl ethyl ketone in water is volatilization (estimated half-times of 3 and 12 days, for rivers and lakes, respectively). Complete aerobic biodegradation of methyl ethyl ketone has been reported in about 5-10 days following inoculation with sewage or polluted surface water. Longer times were required for degradation in marine water. Anaerobic degradation occurred after an acclimation period of about one week (HSDB 1994). Direct photolysis near the surface is also thought to be a possible mechanism, but was not measured (HSDB 1994). It is not expected to undergo chemical hydrolysis or to be bound to sediment or suspended organic matter (HSDB 1994).

4. Biota - Methyl ethyl ketone is not expected to bioconcentrate in fish or aquatic organisms; its estimated fish bioconcentration factor is less than 1 (U.S. EPA 1985).

IV. HUMAN HEALTH EFFECTS

A. Pharmacokinetics

1. Absorption - Studies in humans and animals have demonstrated that methyl ethyl ketone can be absorbed via the lungs, the skin, and the gastrointestinal system. The concentration of methyl ethyl ketone in the atmosphere has been correlated with the alveolar concentration (70% alveolar retention) and blood levels in humans (U.S. EPA 1985). Pulmonary absorption values range from 41.1% to 55.8% (WHO 1993). The relative uptake through the lungs by humans was about 53% through a 4 hour exposure at 200 ppm (HSDB 1994; WHO 1993). Oral studies in rats have demonstrated that the peak blood level of methyl ethyl ketone (0.95 mg/mL) was reached in 4 hours following oral

administration of the chemical in water (1690 mg/kg) (U.S. EPA 1985). Methyl ethyl ketone can also be absorbed through intact human skin. A steady state concentration in expired air was reached in 2-3 hours following exposure of the palmar surface of the forearm of volunteers (Krasavage et al. 1982). Absorption is more rapid through moist skin than through dry skin, and the rate of percutaneous absorption has been estimated to range from 5 to 10 micrograms/cm2/min (WHO 1993).

2. Distribution - The relative solubility of methyl ethyl ketone in various human tissues and organs compared to blood (tissue/blood partition coefficient) was shown to be similar in the kidney, liver, brain, heart, and lung and in fat and muscle tissue. This indicates a potential for even and widespread distribution of methyl ethyl ketone in human tissues (U.S. EPA 1985). It has also been shown to cross the placenta and enter the human fetus (WHO 1993).

3. Metabolism - Experiments with guinea pigs and rats have shown that methyl ethyl ketone is metabolized by oxidative hydroxylation, forming 3-hydroxy-2-butanone, which is further reduced to 2,3-butanediol. Methyl ethyl ketone is also reversibly reduced to 2-butanol (U.S. EPA 1985).

4. Excretion - The half-life of methyl ethyl ketone in the blood of guinea pigs was reported to be 270 minutes, following intraperitoneal injection of 450 mg/kg. The clearance time was 12 hours (U.S. EPA 1985). It has been estimated that humans eliminate 30 to 40% of methyl ethyl ketone intake in expired air (HSDB 1994). The unchanged chemical and its metabolite, 3-hydroxy-2-butanone were measured in the urine of workers occupationally exposed to 8 to 272 mg/m3. The metabolite was only identified in workers exposed to the higher levels, and was correlated with the level of exposure and the urinary concentration of methyl ethyl ketone (U.S. EPA 1985). The plasma half-time in humans has be estimated at 49-96 minutes with an apparent clearance rate of 0.6 L/minute (ATSDR 1992).

B. Acute Toxicity

Acute exposure to moderate to high doses of methyl ethyl ketone can cause headaches, nausea, and irritation of the eyes and respiratory tract; high doses can also result in narcosis. Eye contact with liquid methyl ethyl ketone can cause corneal injury.

1. Humans - Volunteers complained of mild nose and throat irritation when exposed to 100 ppm. The irritation became objectionable when the concentration was raised to 300 ppm (ATSDR 1992). Workers occupationally exposure to an atmosphere containing 300 to 500 ppm (126 to 210 mg/kg/day) (see end note 2) complained of headaches, nausea, and respiratory tract irritation. Momentary exposure to 33,000 or 100,000 ppm caused intolerable irritation of the eyes, nose and throat (Krasavage et al. 1982). Workers exposed either by inhalation (300-600 ppm) or by skin contact to methyl ethyl ketone developed numbness in the extremities and dermatitis. High concentrations can result in central nervous system depression (see Section IV.G.1.). Eye contact with liquid methyl ethyl ketone causes painful irritation, and can result in corneal injury (Krasavage et al. 1982; HSDB 1994).

2. Animals - Oral LD50 values of 2737 and 4050 mg/kg were reported for rats and mice, respectively. Inhalation LC50 values of 23,500 mg/m3/8 hours for rats and 40,000 mg/m3/2 hours for mice were reported (U.S. EPA 1985). Guinea pigs exposed to 10,000 ppm methyl ethyl ketone developed liver and kidney congestion, but no effects were seen at 3500 ppm (ATSDR 1992).

C. Subchronic/Chronic Effects

Human studies have indicated that extended or repeated exposure to relatively high concentrations of methyl ethyl ketone can result in adverse central nervous system effects. Animal studies indicate that extended or repeated inhalation exposure to relatively high concentrations of methyl ethyl ketone can result in hepatic and renal toxicity.

1. Humans - Dermatitis, gastrointestinal upset, loss of appetite and weight, and neurological problems (see Section IV.G.1.) were reported by individuals occupationally exposed to methyl ethyl ketone, apparently in the absence of other solvents (WHO 1993). Neurological problems were also reported by workers chronically exposed to 300-600 ppm of the chemical (WHO 1993). All other available studies describing subchronic/chronic occupational exposure involved a mixture of organic solvents that contained methyl ethyl ketone. A variety of nervous system effects were consistently described after prolonged exposure to these mixtures (see Section IV.G.1.) (WHO 1993).

2. Animals - Male and female Fischer 344 rats were exposed to 0, 1250, 2500, or 5000 ppm methyl ethyl ketone by inhalation 6 hours/day, 5 days/week, for 90 days. No treatment related differences in food consumption, in eye effects, in neurological functioning, or in histopathologies were reported (U.S. EPA 1985). Increased serum alanine amino transferase in females was the only effect at 2500 ppm; increased absolute and relative liver weight were seen in both sexes at 5000 ppm. Females also developed decreased relative brain weight, and increased blood levels of alkaline phosphatase, glucose, and potassium at 5000 ppm. The mean body weights of both sexes were decreased at 5000 ppm, but increased at the other dose levels compared to the controls.

   In another inhalation study Fischer 344 rats were exposed by inhalation to 5041 ppm (14,870 mg/m3), 2518 ppm, or 1254 ppm methyl ethyl ketone for 6 hours/ day, 5 days/week for 90 days. No significant effects on food consumption, eyes, or morphology were observed (WHO 1993). Increased absolute and relative liver weight, decreased body weight, increased relative kidney weight, decreased relative brain and spleen weights, and increased mean corpuscular hemoglobin were reported at the high dose. Increased body weights were reported at the low and intermediate dose.

   Male rats exposed to 10,000 ppm methyl ethyl ketone 8 hours/day, 7 days/week developed severe irritation in the upper respiratory tract within a few days and died during the 7th week of exposure of bronchopneumonia (ATSDR 1992).

D. Carcinogenicity

There is inadequate information to evaluate the carcinogenicity of

methyl ethyl ketone in humans and in laboratory animals.

1. Humans - No excess cancer incidence was found in an epidemiological study of 446 male workers in two methyl ethyl ketone dewaxing plants. The deaths observed were below the expected, and overall deaths from cancer were also below the expected. An increase in tumors of the buccal cavity and pharynx was seen but the numbers were small (2 observed, 0.13 expected) and lung cancers were significantly decreased (1 observed, 6.02 expected) (ATSDR 1992; WHO 1993). The overall cancer-related mortality was less than expected in another epidemiological study of 1008 male oil refinery workers exposed to 1-4 ppm methyl ethyl ketone. There were no increases in buccal and pharyngeal cancers seen in this study (ATSDR 1992).

2. Animals - Methyl ethyl ketone was applied to the skin of mice twice weekly for one year (50 mg/dose). No tumors were reported (U.S. EPA 1989). No information on the carcinogenicity of methyl ethyl ketone by other routes of administration were found in the secondary sources searched.

E. Genotoxicity

Results from four out of the five short term mutagenicity assays, requested by and submitted to EPA under the Toxic Substances Control Act (TSCA), indicate methyl ethyl ketone is not mutagenic. Methyl ethyl ketone is negative in the Ames test (in Salmonella typhimurium strains TA98, TA100, TA1535, and TA1537 with or without S-9 metabolic activation); the mouse lymphoma test; the cell transformation assay; and the mouse micronucleus test. Results from the Section 4 unscheduled DNA test was concluded to be positive (Cimino 1985).

Most of the information from other secondary sources also indicate that methyl ethyl ketone is not genotoxic. Methyl ethyl ketone was negative in E. coli tester strains WP2 and WP2uvrA (WHO 1993). It was negative in the mitotic gene conversion assay in S. cerevisiae tester strain JD1 (WHO 1993). It was negative in the micronucleus test in both CD1 mice and Chinese hamsters (WHO 1993). It was a strong inducer of aneuploidy in S. cerevisiae strain D61.M (U.S. EPA 1989).

F. Developmental/Reproductive Toxicity

Animal studies indicate that exposure to high methyl ethyl ketone concentrations in air breathed during pregnancy can cause fetal toxicity and possibly adverse developmental effects. EPA has derived an oral reference dose (RfD) (see end note 3) of 0.6 mg/kg/day, based on developmental effects of a metabolite (2-butanol) of MEK. EPA has derived an inhalation reference concentration (RfC) (see end note 4) of 1 mg/m3 for methyl ethyl ketone, based on its developmental effects.

1. Humans - No information on the developmental/reproductive toxicity of methyl ethyl ketone was found in the secondary sources searched.

2. Animals - Since there are no appropriate oral studies on methyl ethyl ketone, the U.S. EPA (1994) calculated a chronic oral RfD for methyl ethyl ketone of 0.6 mg/kg/day, based on decreased birth weights seen in a multigeneration study with its metabolic intermediate, 2-butanol. Male and female Wistar rats (30/sex/

group) were given 2-butanol in drinking water at 0, 0.3, 1.0, or 3.0% nine weeks before mating through gestation and lactation. The high dose was reduced to 2.0% for the second generation. Decreased fetal weight and decreased pup survivability were reported for the first generation at 3.0% 2-butanol. Decreased fetal weight was seen in the second generation at 2.0%. Increases in the incidences of missing sternebrae, wavy ribs, and incomplete vertebrae ossification at 2%, compared to the 1.0 and 0.3% groups, were seen. However, because of high incidences of these developmental effects in the control group, they could not be determined to be treatment related. The 1.0% dose, equivalent to 1771 mg/kg/day, was identified as a no-adverse-effect-level (NOAEL), and the 2.0% dose was identified as a lowest-adverse-effect-level (LOAEL) (U.S. EPA 1994).

The U.S. EPA (1994) calculated a chronic inhalation reference concentration (RfC) of 1.0 mg/m3 for methyl ethyl ketone, based on decreased fetal birth weight seen in a mouse inhalation study. Pregnant mice were exposed by inhalation to atmospheric concentrations of 0, 398, 1010, or 3020 ppm methyl ethyl ketone 7 hours/day during days 6-15 of gestation. Decreased fetal body weight was seen at 3020 ppm. There was an increased incidence of fetuses and litters with malformations in the treated groups, but the increases were not statistically significant. A NOAEL of 1010 ppm and a LOAEL of 3020 ppm were identified (U.S. EPA 1994).

Groups of 25 pregnant Sprague-Dawley rats were exposed to air concentrations of 400, 1000, or 3000 ppm methyl ethyl ketone 7 hours/day during days 6-15 of gestation. The control group contained 35 rats. Maternal body weight gain was decreased and water consumption was increased in dams receiving 3000 ppm. There were no treatment related effects on the pregnancy rate, the number of implantations per litter, or the percent live fetuses. A total of five fetuses with at least one external or soft tissue malformation were reported, but were distributed in all groups including the control. Increased incidences of delayed ossification and extra ribs at the 3000 ppm dose were attributed to fetal toxicity (U.S. EPA 1989).

G. Neurotoxicity

Neurological effects, observed in humans and animals exposed to high concentrations of methyl ethyl ketone, appear to be reversible. Concentrations high enough to cause central nervous system depression also cause severe pulmonary irritation.

1. Humans - American workers exposed to 300-600 ppm methyl ethyl ketone reported numbness in the fingers and toes. Italian workers chronically exposed to the chemical developed reduced nerve conduction velocities, headaches, dizziness, and muscle hypotrophy (WHO 1993).

   Most reports involving human exposure to methyl ethyl ketone describe effects seen after exposure to mixtures of solvents. Methyl ethyl ketone has been shown to potentiate the effects of other solvents, especially n-hexane (U.S. EPA 1989). Workers exposed to a mixture containing methyl ethyl ketone (39 ppm), n-hexane (90 ppm), cyclohexane (92 ppm), and ethyl acetate (57 ppm) complained of sleepiness, dizziness weakness, paraesthesia, and hypo-aesthesia (WHO 1993). Reductions in the maximal motor and distal sensory nerve conduction velocities in

the median and ulnar nerves and decreased maximal motor nerve conduction velocity in the peroneal nerve were reported after 2-8 years exposure to a mixture containing methyl ethyl ketone (60 ppm), n-hexane (196 ppm), cyclohexane (170 ppm) and ethyl acetate (100 ppm). The latency of sensory peak action potentials were increased and the amplitude of peripheral nerve action potentials were decreased. The effects were attributed to n-hexane, possibly potentiated by methyl ethyl ketone (WHO 1993).

2. Animals - Wistar rats exposed to 200 ppm (roughly equivalent to 244 mg/kg/dy) methyl ethyl ketone 12 hours/day, 7 days/week, for 24 weeks exhibited transient increases in motor nerve conduction velocities and decreased distal motor latency. These effects were observed after four weeks of exposure but not after 12 weeks (U.S. EPA 1989). Transient behavioral changes were reported in baboons exposed to 100 ppm for 7 days. Intravenous infusion of 5 mg/kg methyl ethyl ketone per hour into Sprague-Dawley rats resulted in depression of the vestibulo-oculomotor reflex. Depression of the central nervous system followed with continued infusion (WHO 1993). No neuropathology or histological changes were found in several experiments in chickens, cats, rats, and mice exposed to atmospheres containing up to 1500 ppm for up to 12 weeks. Exposure to high concentrations results in narcosis.

Guinea pigs exposed to an atmospheric concentration of 10,000 ppm experience narcosis in four to five hours; however, irritation of the eyes and nose develops within four minutes (Krasavage et al. 1982).

V. ENVIRONMENTAL EFFECTS

The toxicity of methyl ethyl ketone in aquatic organisms is low; toxicity values are greater than 100 mg/L. It also has low toxicity in terrestrial rodents for inhalation exposure.

A. Toxicity to Aquatic Organisms

24 Hour LC50 values for fish are: >5000 mg/L for Carassius auratus (goldfish); >400 mg/L for Cyprinodon variegatus (sheepshead minnow); and 5640 mg/L for Lepomis macrochirus (bluegill) (AQUIRE 1994). 96 Hours LC50 values for fish include: 3200 mg/L for Pimephales promelas (fathead minnow); 5600 mg/L for Gambusia affinis (mosquito fish); and 4467 mg/L for Lepomis macrochirus (bluegill) (WHO 1993). 24 Hour LC50 values of 8890 mg/L for Daphnia magna (water flea) and 1950 mg/L for Artemia salina (brine shrimp) were reported (WHO 1993).

B. Toxicity to Terrestrial Organisms

The toxicity information reported for rats and rabbits (see sections IV.B.2. and IV.C.2.) suggests that no adverse effects would be seen at expected environmental concentrations.

C. Abiotic Effects

Methyl ethyl ketone is known to contribute to photochemical smog episodes (Federal Register 1992). Smog chamber studies indicate that methyl ethyl ketone is of intermediate reactivity with degradation rates ranging from 1.5% in one hour to 33% in 6.5 hour (HSDB 1994).

VI. EPA/OTHER FEDERAL ACTIVITY

Voluntary reduction of methyl ethyl ketone environmental releases has occurred since 1991, as a result of a joint industry/EPA pollution prevention initiative known as the 33/50 program. The 1990 Clean Air Act Amendments list methyl ethyl ketone as a hazardous air pollutant. Occupational exposure to methyl ethyl ketone is regulated by the Occupational Safety and Health Administration (OSHA). The permissible exposure limit (PEL) is 200 parts per million parts of air (ppm) as an 8-hour time-weighted average (TWA) (29 CFR 1910.1000) (Mannsville 1993).

Federal agencies/other groups that can provide additional information on methyl ethyl ketone are listed in Table 4 and 5.

TABLE 4. EPA OFFICES AND CONTACT NUMBERS FOR INFORMATION ON METHYL ETHYL KETONE

EPA OFFICE	LAW	PHONE NUMBER
Pollution Prevention & Toxics	Toxic Substances Control Act (Sec. 4/8A/8D)	(202) 554-1404
	Emergency Planning and Community Right-to-Know Act (EPCRA) Regulations (Sec. 313)	(800) 535-0202
	Toxics Release Inventory data	(202) 260-1531
Air	Clean Air Act	(919) 541-0888
Solid Waste & Emergency Response	Comprehensive Environmental Response, Compensation, and Liability Act (Superfund)/ Resource Conservation and Recovery Act / EPCRA (Sec. 304/311/312)	(800) 535-0202
Water	Safe Drinking Water Act	(800) 426-4791

TABLE 5. OTHER FEDERAL OFFICE/OTHER GROUP CONTACT NUMBERS FOR INFORMATION ON METHYL ETHYL KETONE

Other Agency/Department/Other Group	Contact Number
Agency for Toxic Substances & Disease Registry	(404) 639-6000
American Conference of Governmental Industrial Hygienists Recommended TLV-TWA: 200 ppm; TLV-STEL 300 ppm (see end note 7) (ACGIH 1991)	(513) 742-2020
Consumer Product Safety Commission	(301) 504-0994
Food & Drug Administration	(301) 443-3170
National Institute for Environmental Health Sciences (EnviroHealth Clearinghouse)	(800) 643-4794
National Institute for Occupational Safety & Health Recommended TWA: 200 ppm; STEL 300 ppm; IDLH, 3000 ppm (see end note 5) (NIOSH 1992)	(800) 356-4674
Occupational Safety & Health Administration Permissible TWA: 200 ppm (see end note 6) (OSHA 1993)	Check local phone book for phone number under Department of Labor

VII. END NOTES

1. Standard Industrial Classification code is the statistical classification standard for all Federal economic statistics. The code provides a convenient way to reference economic data on industries of interest to the researcher. SIC codes presented here are not intended to be an exhaustive listing; rather, the codes listed should provide an indication of where a chemical may be most likely to be found in commerce.

2. Calculated using the factor, 2.94 (Verschueren 1983), to convert ppm to mg/m3, which is multiplied by 0.1429 (the occupational 8-hour breathing rate, 10 m3, divided by the assumed adult body weight, 70 kg) to obtain the dose in mg/kg/day assuming 100% absorption (U.S. EPA 1988).

3. The RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of the daily exposure level for the human population, including sensitive subpopulations, that is likely to be without an appreciable risk of deleterious effects during the time period of concern.

4. An inhalation reference concentration is an estimate (with uncertainty spanning perhaps an order of magnitude) of the exposure level for the human population, including sensitive populations, that is likely to be without an appreciable risk of deleterious effects during the time period of concern.

5. TWA, occupational, Time Weighted Average; STEL, occupational, Short Term Exposure Limit, 15 min.; IDLH, Immediate Danger to Life and Health.

6. PEL-TWA, Permissible Exposure Limit-Time Weighted Average

7. TLV-TWA, Threshold Limit Value-Time Weighted Average; TLV-STEL, Threshold Limit Value-Short Term Exposure Limit

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Environmental Health Center National Safety Council

Environment Writer

Chemical Backgrounders

These chemical backgrounders have been updated and moved to the National Safety Council's Crossroads page. These backgrounders provide descriptions, chemical properties, health effects, economics, and regulations on various hazardous chemicals. Please update your bookmark and click on the link above if your browser does not refresh in 5 seconds.

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CHEMICALS

Select a Chemical Backgrounder:

1,1,1-Trichloroethane
1,1,2,2-Tetrachloroethane
1,1-Dichloroethane
1,2,3-Trichloropropane
1,3-Butadiene
1,4-Dichlorobenzene
2,4-Dinitrotoluene
2,6-Dinitrotoluene
2-Nitropropane
3,3-Dichlorobenzidine
4,4'-Isopropylidenediphenol

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Features

Exposure Guidelines
By: *Nir Barnea*
National Oceanic and Atmospheric Administration, OR&R (formerly NOAA/HAZMAT)

Emergency response guidelines are often needed during a spill incident, in order to help determine the level of concern (LOC) in case of a possible population exposure. The LOC selected may greatly affect the response activity. [more...]

Highlights

Chemical Reactivity Series:

- Chemical Reactivity Issues
- Chemical Hazards Produced by Water-Reactive Substance
- The Powell Duffryne Explosion: A Case History

Resources

Chemical Reactivity Worksheets Free software from EPA and NOAA to virtually "mix" chemicals to identify the reactivity of substances or mixtures.

RMP*Comp - Free EPA program to complete offsite consequence analyses.

Agency for Toxic Substances and Disease Registry's- (ATSDR) top 20 hazardous substances



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International Chemical Safety Cards

METHYL ETHYL KETONE

ICSC: 0179

METHYL ETHYL KETONE
Ethyl methyl ketone
2-Butanone
MEK
Methyl acetone
C_4H_8O / $CH_3COCH_2CH_3$
Molecular mass: 72.1

CAS # 78-93-3
RTECS # EL6475000
ICSC # 0179
UN # 1193
EC # 606-002-00-3



TYPES OF HAZARD/ EXPOSURE	ACUTE HAZARDS/ SYMPTOMS	PREVENTION	FIRST AID/ FIRE FIGHTING
FIRE	Highly flammable.	NO open flames, NO sparks, and NO smoking.	Powder, AFFF, foam, carbon dioxide.
EXPLOSION	Vapour/air mixtures are explosive.	Closed system, ventilation, explosion-proof electrical equipment and lighting. Do NOT use compressed air for filling, discharging, or handling. Use non-sparking handtools.	In case of fire: keep drums, etc., cool by spraying with water.
EXPOSURE			
• **INHALATION**	Cough. Dizziness. Drowsiness. Headache. Nausea. Vomiting.	Ventilation, local exhaust, or breathing protection.	Fresh air, rest. Refer for medical attention.
• **SKIN**		Protective gloves.	Remove contaminated clothes. Rinse skin with plenty of water or shower.
• **EYES**	Redness. Pain.	Safety goggles.	First rinse with plenty of water for several minutes (remove contact lenses if easily possible), then take to a doctor.

• **INGESTION**	Unconsciousness. (Further see Inhalation).	Do not eat, drink, or smoke during work.	Rinse mouth. Give plenty of water to drink. Refer for medical attention.

SPILLAGE DISPOSAL	STORAGE	PACKAGING & LABELLING
Collect leaking and spilled liquid in sealable containers as far as possible. Absorb remaining liquid in sand or inert absorbent and remove to safe place. Do NOT wash away into sewer. (extra personal protection: self-contained breathing apparatus).	Fireproof. Separated from strong oxidants, strong acids. Cool. Well closed.	F symbol Xi symbol R: 11-36/37 S: (2-)9-16-25-33 UN Hazard Class: 3 UN Packing Group: II

SEE IMPORTANT INFORMATION ON BACK

ICSC: 0179

Prepared in the context of cooperation between the International Programme on Chemical Safety & the Commission of the European Communities © IPCS CEC 1993 No modifications to the International version have been made except to add the OSHA PELs, NIOSH RELs and IDLH values.

International Chemical Safety Cards

METHYL ETHYL KETONE

ICSC: 0179

IMPORTANT DATA

PHYSICAL STATE; APPEARANCE:
COLOURLESS LIQUID , WITH CHARACTERISTIC ODOUR.

PHYSICAL DANGERS:
The vapour is heavier than air and may travel along the ground; distant ignition possible.

CHEMICAL DANGERS:
Reacts violently with strong oxidants and inorganic acids, causing fire and explosion hazard. Attacks some plastics.

OCCUPATIONAL EXPOSURE LIMITS (OELs):
TLV (as TWA): 200 ppm; 590 mg/m^3; as STEL: 300 ppm; 885 mg/m^3 (ACGIH 1997).
MAK: 200 ppm; 590 mg/m^3; D (1992)
OSHA PEL: TWA 200 ppm (590 mg/m^3)
NIOSH REL: TWA 200 ppm (590 mg/m^3) ST 300 ppm (885 mg/m^3)
NIOSH IDLH: 3000 ppm

ROUTES OF EXPOSURE:
The substance can be absorbed into the body by inhalation and by ingestion.

INHALATION RISK:
A harmful contamination of the air can be reached rather quickly on evaporation of this substance at 20°C.

EFFECTS OF SHORT-TERM EXPOSURE:
The substance irritates the eyes and the respiratory tract. The substance may cause effects on the central nervous system. Exposure far above the OEL may result in unconsciousness.

EFFECTS OF LONG-TERM OR REPEATED EXPOSURE:
The liquid defats the skin. Animal tests show that this substance possibly causes toxic effects upon human reproduction.

PHYSICAL PROPERTIES	Boiling point: 80°C Melting point: -86°C Relative density (water = 1): 0.8 Solubility in water, g/100 ml at 20°C: 29 Vapour pressure, kPa at 20°C: 10.5 Relative vapour density (air = 1): 2.41	Relative density of the vapour/air-mixture at 20°C (air = 1): 1.1 Flash point: -9°C (c.c.) Auto-ignition temperature: 505°C Explosive limits, vol% in air: 1.8-11.5 Octanol/water partition coefficient as log Pow: 0.29
ENVIRONMENTAL DATA		

N O T E S

The odour warning when the exposure limit value is exceeded is insufficient.

Transport Emergency Card: TEC (R)-88.
NFPA Code: H1; F3; R0.

ADDITIONAL INFORMATION

ICSC: 0179 **METHYL ETHYL KETONE**

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Level 1

Chemical Name: Methyl Ethyl Ketone

CAS Registry Number: 78-93-3

Click on red circle(s) to obtain data.

Risk Value	ATSDR	Health Canada	ITER	RIVM	U.S.EPA	WHO/IPCS
Noncancer Oral	●	●	●	●	●	●
Cancer Oral	●	●	●	●	●	●
Noncancer Inhalation	●	●	●	●	●	●
Cancer Inhalation	●	●	●	●	●	●

Glossary of ITER definitions

ITER Instructions

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Toxicology Excellence for Risk Assessment

TERA

NTP CHEMICAL REPOSITORY (RADIAN CORPORATION, AUGUST 29, 1991)
METHYL ETHYL KETONE

-IDENTIFIERS
 ===========

*CATALOG ID NUMBER: 001254

*CAS NUMBER: 78-93-3

*BASE CHEMICAL NAME: METHYLETHYLKETONE

*PRIMARY NAME: METHYL ETHYL KETONE

*CHEMICAL FORMULA: C4H8O

*STRUCTURAL FORMULA: CH3COCH2CH3

*WLN: 2V1

*SYNONYMS:
  2-BUTANONE
  BUTANONE
  ETHYL METHYL KETONE
  KETONE, ETHYL METHYL
  METHYL ACETONE
  MEK
  MEETCO
  RCRA WASTE NUMBER U159
  UN 1193
  UN 1232

-PHYSICAL CHEMICAL DATA
 ======================

*PHYSICAL DESCRIPTION: LITERATURE: Clear colorless liquid
REPOSITORY: Clear colorless liquid

*MOLECULAR WEIGHT: 72.11

*SPECIFIC GRAVITY: 0.805 @ 20/4 C [031,055,062,421]

*DENSITY: 0.806 g/mL @ 20 C [371]

*MP (DEG C): -86.3 C [017,047,371]

*BP (DEG C): 79.6 C [017,031,055,205,371]

*SOLUBILITIES:
WATER : >=100 mg/mL @ 19 C (RAD)

DMSO : >=100 mg/mL @ 19 C (RAD)

95% ETHANOL : >=100 mg/mL @ 19 C (RAD)

METHANOL : Not available

ACETONE : >=100 mg/mL @ 19 C (RAD)

TOLUENE : Not available

OTHER SOLVENTS:
Benzene: Miscible [031,205]
Ether: Miscible [031,205]
Industrial organic solvents: Soluble [421]
Oils: Miscible [062]

*VOLATILITY:
Vapor pressure: 77.5 mm Hg @ 20 C [055,421,430]; 100 mm Hg @ 25.0 C [038]
Vapor density : 2.42 [043]

*FLAMMABILITY(FLASH POINT):
This chemical has a flash point of -3 C (26 F) [205,269,275]. It is flammable. Fires involving this material can be controlled with a dry chemical, carbon dioxide or Halon extinguisher. A water spray may also be used [036,269,451]. The autoignition temperature is 515 C (960 F) [036,043,051,062, 421].

*UEL: 10% [036,051,062] LEL: 1.8% [043,058,066,430]

*REACTIVITY:
This chemical is incompatible with strong oxidizers [058,269,346]. It is also incompatible with chlorosulfonic acid, oleum, hydrogen peroxide, and nitric acid [043]. It can react with potassium tert-butoxide and with chloroform [043,066]. It can also react with bases and strong reducing agents [269]. Vigorous reactions occur with chloroform in the presence of bases, and explosive peroxides are formed with (hydrogen peroxide + nitric acid) [036]. It is also incompatible with 2-propanol [066].

*STABILITY:
This chemical is stable under normal laboratory conditions. Solutions of this chemical in water, DMSO, 95% ethanol or acetone should be stable for 24 hours under normal lab conditions (RAD).

*OTHER PHYSICAL DATA:
Specific gravity: 0.7997 @ 25/4 C; 0.8255 @ 20/4 C [062]
Specific gravity: 0.80615 @ 20/20 C [043,051]
Boiling point: 30 C @ 119 mm Hg [017]
Refractive index: 1.3788 @ 20 C [047]; 1.3814 @ 15 C [026]
Fragrant, mint-like, moderately sharp odor [346]
Odor threshold: 2 ppm [055,430]
log P octanol: 0.26 [055]
Specific heat: 0.549 cal/g [062]
Viscosity: 0.40 centipoise @ 25 C [062]
Constant boiling mixture with water (88.7%) with a boiling point of 73.4 C [[031]
Lambda max: 400-350 nm, 340 nm, 330 nm (A=0.01, 0.10, 1.0) [275]

-TOXICITY
========

*NIOSH REGISTRY NUMBER: EL6475000

*TOXICITY:

typ. dose	mode	specie	amount	units	other
TCLo	ihl	hmn	100	ppm/5M	
LC50	ihl	mus	40	gm/m3/2H	
LC50	ihl	rat	23500	mg/m3/8H	
LDLo	ipr	gpg	2000	mg/kg	

LD50	ipr	mus	616	mg/kg
LD50	orl	mus	4050	mg/kg
LD50	orl	rat	2737	mg/kg
LD50	skn	rbt	6480	mg/kg
LC50	ihl	mam	38	gm/m3
LD50	ipr	rat	607	mg/kg

*AQTX/TLM96: over 1000 ppm

*SAX TOXICITY EVALUATION:
THR: Moderately toxic by ingestion, skin contact and intraperitoneal routes. Human systemic effects by inhalation. An experimental teratogen. Experimental reproductive effects. A strong irritant. Human eye irritation @ 350 ppm. Affects peripheral nervous system and central nervous system.

*CARCINOGENICITY: Not available

*MUTATION DATA:

test	lowest dose	test	lowest dose
sln-smc	33800 ppm		

*TERATOGENICITY:
Reproductive Effects Data:
TCLo: ihl-rat 3000 ppm/7H (6-15D preg)
TCLo: ihl-rat 1000 ppm/7H (6-15D preg)

*STANDARDS, REGULATIONS & RECOMMENDATIONS:
OSHA: Federal Register (1/19/89) and 29 CFR 1910.1000 Subpart Z
Transitional Limit: PEL-TWA 200 ppm [610]
Final Limit: PEL-TWA 200 ppm; STEL 300 ppm [610]
ACGIH: TLV-TWA 200 ppm; STEL 300 ppm [015,415,421,610]
NIOSH Criteria Document: Recommended Exposure Limit to this compound-air: TWA 200 ppm [610]
NFPA Hazard Rating: Health (H): 1
Flammability (F): 3
Reactivity (R): 0
H1: Materials only slightly hazardous to health (see NFPA for details).
F3: Materials which can be ignited under almost all normal temperature conditions (see NFPA for details).
R0: Materials which are normally stable even under fire exposure conditions and which are not reactive with water (see NFPA for details).

*OTHER TOXICITY DATA:
Skin and Eye Irritation Data:
eye-hmn 350 ppm
skn-rbt 500 mg/24H MOD
skn-rbt 402 mg/24H MLD
skn-rbt 13780 ug/24H open MLD
eye-rbt 80 mg
Review: Toxicology Review
Standards and Regulations: DOT-Hazard: Flammable liquid; Label: Flammable liquid
Status: EPA Genetox Program 1988, Inconclusive: B subtilis rec assay
EPA TSCA Chemical Inventory, 1986
EPA TSCA 8(a) Preliminary Assessment Information, Final Rule
EPA TSCA Test Submission (TSCATS) Data Base, January 1989
NIOSH Analytical Methods: see 2-Butanone, 2500
NIOSH Analytical Methods: see 2-Butanone, Ethanol, and Toluene in blood, 8002

Meets criteria for proposed OSHA Medical Records Rule

-OTHER DATA (Regulatory)
 ========================

*PROPER SHIPPING NAME (IATA): Ethyl methyl ketone

*UN/ID NUMBER: UN1193

*HAZARD CLASS: 3 SUBSIDIARY RISK: None PACKING GROUP: II

*LABELS REQUIRED: Flammable liquid

*PACKAGING: PASSENGER: PKG. INSTR.: 305, Y305 MAXIMUM QUANTITY: 5 L, 1 L
CARGO : PKG. INSTR.: 307 MAXIMUM QUANTITY: 60 L

*SPECIAL PROVISIONS: None

*USES:
This compound is used as a solvent in nitrocellulose coating and vinyl film manufacture, in smokeless powder manufacture, in cements and adhesives, dewaxing of lubricating oils, "Glyptal" resins, paint removers, organic synthesis, cleaning fluids, acrylic coatings; intermediate in drug manufacture; manufacture of colorless synthetic resins; swelling agent of resins; intermediate in the manufacture of ketones and amines; and printing catalyst and carrier.

*COMMENTS: Not available

-HANDLING PROCEDURES
 ====================

*ACUTE/CHRONIC HAZARDS:
This compound may be harmful by inhalation, ingestion or skin absorption. It is a severe irritant of the skin and eyes [269]. It is also an irritant of the mucous membranes and upper respiratory tract [151,269]. When heated to decomposition it emits toxic fumes of carbon monoxide and carbon dioxide [269].

*MINIMUM PROTECTIVE CLOTHING: Not available

*RECOMMENDED GLOVE MATERIALS:
Permeation Test Results For The Neat (Undiluted) Chemical:
The permeation test results for the neat (undiluted) chemical are given below. The breakthrough times of this chemical are given for each glove type tested. The table is a presentation of actual test results, not specific recommendations or suggestions. Avoid glove types which exhibit breakthrough times of less than the anticipated task time plus an adequate safety factor. If this chemical makes direct contact with your glove, or if a tear, puncture or hole develops, replace them at once.

Glove Type	Model Number	Thickness	Breakthrough Time
Butyl rubber	North B-174	0.61 mm	480 min
PVA	Edmont 25-545	0.69 mm	320 min
Neoprene	Edmont 29-870	0.51 mm	10 min
Latex	Ackwell 5-109	0.13 mm	1 min

*RECOMMENDED RESPIRATOR:
When working with this chemical, wear a NIOSH-approved full face chemical cartride respirator equipped with the appropriate organic vapor

cartridges. If that is not available, a half face respirator similarly equipped plus airtight goggles can be substituted. However, please note that half face respirators provide a substantially lower level of protection than do full face respirators.

*OTHER: Not available

*STORAGE PRECAUTIONS:
You should store this chemical in an explosion-proof refrigerator and keep it away from oxidizing materials. STORE AWAY FROM SOURCES OF IGNITION.

*SPILLS AND LEAKAGE:
If you spill this chemical, FIRST REMOVE ALL SOURCES OF IGNITION. Then, use absorbent paper to pick up all liquid spill material. Seal the absorbent paper, as well as any of your clothing which may be contaminated, in a vapor-tight plastic bag for eventual disposal. Wash any surfaces you may have contaminated with a soap and water solution. Do not reenter the contaminated area until the Safety Officer (or other responsible person) has verified that the area has been properly cleaned.

*DISPOSAL AND WASTE TREATMENT: Not available

-EMERGENCY PROCEDURES
==========

*SKIN CONTACT:
IMMEDIATELY flood affected skin with water while removing and isolating all contaminated clothing. Gently wash all affected skin areas thoroughly with soap and water.
If symptoms such as redness or irritation develop, IMMEDIATELY call a physician and be prepared to transport the victim to a hospital for treatment.

*INHALATION:
IMMEDIATELY leave the contaminated area; take deep breaths of fresh air. If symptoms (such as wheezing, coughing, shortness of breath, or burning in the mouth, throat, or chest) develop, call a physician and be prepared to transport the victim to a hospital.
Provide proper respiratory protection to rescuers entering an unknown atmosphere. Whenever possible, Self-Contained Breathing Apparatus (SCBA) should be used; if not available, use a level of protection greater than or equal to that advised under Respirator Recommendation.

*EYE CONTACT:
First check the victim for contact lenses and remove if present. Flush victim's eyes with water or normal saline solution for 20 to 30 minutes while simultaneously calling a hospital or poison control center.
Do not put any ointments, oils, or medication in the victim's eyes without specific instructions from a physician.
IMMEDIATELY transport the victim after flushing eyes to a hospital even if no symptoms (such as redness or irritation) develop.

*INGESTION:
DO NOT INDUCE VOMITING. Volatile chemicals have a high risk of being aspirated into the victim's lungs during vomiting which increases the medical problems.
If the victim is conscious and not convulsing, give 1 or 2 glasses of water to dilute the chemical and IMMEDIATELY call a hospital or poison control center. IMMEDIATELY transport the victim to a hospital.
If the victim is convulsing or unconscious, do not give anything by mouth,

ensure that the victim's airway is open and lay the victim on his/her side with the head lower than the body. DO NOT INDUCE VOMITING. IMMEDIATELY transport the victim to a hospital.

*SYMPTOMS:

Symptoms of exposure to this compound may include severe irritation of the eyes, irritation of the skin and upper respiratory tract, headache, dizziness and nausea [058,269]. Other symptoms may include weakness, fatigue, possible respiratory arrest, diarrhea, vomiting, stomach and/or intestinal irritation and unconsciousness [058]. It may cause irritation of the nose and throat, diminished vision, mild vertigo and narcosis [430]. It may also cause central nervous system effects and neuropathy [301]. It may irritate the mucous membranes [151]. Prolonged exposure may produce central nervous system depression [430]. Repeated exposure is reported to cause permanent brain and nervous system damage [058]. Eye contact may result in slight conjunctival hyperemia developing to severe anterior uveitis [099]. It may also result in corneal injury. Prolonged skin contact may defat the skin and produce dermatitis [430]. A drop in rabbit eyes has produced moderate reversible injury [099].

-SOURCES
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New Jersey Department of Health and Senior Services

HAZARDOUS SUBSTANCE FACT SHEET

Common Name: **METHYL ETHYL KETONE**

CAS Number: 78-93-3
DOT Number: UN 1193

RTK Substance number: 1258
Date: February 1989 Revision: September 1996

HAZARD SUMMARY

* **Methyl Ethyl Ketone** can affect you when breathed in and by passing through your skin.
* **Methyl Ethyl Ketone** can irritate the skin causing a rash and burning feeling on contact. Repeated exposure can cause drying and cracking of the skin.
* Contact can severely irritate and burn the eyes, leading to permanent damage.
* Exposure to the vapor can irritate the eyes, nose, mouth, and throat causing coughing and wheezing.
* Exposure can cause dizziness, lightheadedness, headache, nausea, blurred vision, and may cause you to pass out.
* Repeated exposure can damage the nervous system and may affect the brain.
* **Methyl Ethyl Ketone** is a FLAMMABLE LIQUID.

IDENTIFICATION

Methyl Ethyl Ketone is a colorless liquid with a fragrant, mint-like odor. It is used as a solvent and in making plastics, textiles, and paints.

REASON FOR CITATION

* **Methyl Ethyl Ketone** is on the Hazardous Substance List because it is regulated by OSHA and cited by ACGIH, DEP, DOT, NIOSH, NFPA, HHAG and EPA.
* Definitions are provided on page 5.

HOW TO DETERMINE IF YOU ARE BEING EXPOSED

The New Jersey Right to Know Act requires most employers to label chemicals in the workplace and requires public employers to provide their employees with information and training concerning chemical hazards and controls. The federal OSHA Hazard Communication Standard, 1910.1200, requires private employers to provide similar training and information to their employees.

* Exposure to hazardous substances should be routinely evaluated. This may include collecting air samples. Under OSHA 1910.20, you have a legal right to obtain copies of sampling results from your employer.
* If you think you are experiencing any work-related health problems, see a doctor trained to recognize occupational diseases. Take this Fact Sheet with you.

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* **ODOR THRESHOLD = 5.4 ppm**.
* The range of accepted odor threshold values is quite broad. Caution should be used in relying on odor alone as a warning of potentially hazardous exposures.

WORKPLACE EXPOSURE LIMITS

OSHA: The legal airborne permissible exposure limit (PEL) is **200 ppm** averaged over an 8-hour workshift.

NIOSH: The recommended airborne exposure limit is **200 ppm** averaged over a 10-hour workshift and **300 ppm** not to be exceeded during any 15 minute work period.

ACGIH: The recommended airborne exposure limit is **200 ppm** averaged over an 8-hour workshift and **300 ppm** as a STEL (short term exposure limit).

* The above exposure limits are for air levels only. When skin contact also occurs, you may be overexposed, even though air levels are less than the limits listed above.

WAYS OF REDUCING EXPOSURE

* Where possible, enclose operations and use local exhaust ventilation at the site of chemical release. If local exhaust ventilation or enclosure is not used, respirators should be worn.
* Wear protective work clothing.
* Wash thoroughly immediately after exposure to **Methyl Ethyl Ketone** and at the end of the workshift.
* Post hazard and warning information in the work area. In addition, as part of an ongoing education and training effort, communicate all information on the health and safety hazards of **Methyl Ethyl Ketone** to potentially exposed workers.

This Fact Sheet is a summary source of information of all potential and most severe health hazards that may result from exposure. Duration of exposure, concentration of the substance and other factors will affect your susceptibility to any of the potential effects described below.

HEALTH HAZARD INFORMATION

Acute Health Effects

The following acute (short-term) health effects may occur immediately or shortly after exposure to **Methyl Ethyl Ketone**:

* **Methyl Ethyl Ketone** can irritate the skin causing a rash and burning feeling on contact.
* Contact can severely irritate and burn the eyes, leading to permanent damage.
* Exposure to the vapor can irritate the eyes, nose, mouth, and throat causing coughing and wheezing.
* Exposure can cause dizziness, lightheadedness, headache, nausea, blurred vision, and may cause you to pass out.

Chronic Health Effects

The following chronic (long-term) health effects can occur at some time after exposure to **Methyl Ethyl Ketone** and can last for months or years:

Cancer Hazard

* According to the information presently available to the New Jersey Department of Health and Senior Services, **Methyl Ethyl Ketone** has not been tested for its ability to cause cancer in animals.

Reproductive Hazard

* There is limited evidence that **Methyl Ethyl Ketone** is a teratogen in animals. Until further testing has been done, it should be treated as a possible teratogen in humans.

Other Long-Term Effects

* Repeated exposure can damage the nervous system and may affect the brain. Effects may include reduced memory and concentration, personality changes (withdrawal, irritability), fatigue, sleep disturbances, reduced coordination, and/or effects on nerves supplying internal organs (autonomic nerves) and/or nerves to the arms and legs (weakness, "pins and needles").
* Repeated exposure can cause drying and cracking of the skin.

MEDICAL

Medical Testing

If symptoms develop or overexposure is suspected, the following may be useful:

* Interview for brain effects, including recent memory, mood (irritability, withdrawal), concentration, headaches, malaise and altered sleep patterns. Consider cerebellar, autonomic and peripheral nervous system evaluation. Positive and borderline individuals should be referred for neuropsychological testing.

Any evaluation should include a careful history of past and present symptoms with an exam. Medical tests that look for damage already done are not a substitute for controlling exposure.

Request copies of your medical testing. You have a legal right to this information under OSHA 1910.20.

Mixed Exposures

Methyl Ethyl Ketone in combination with *Methyl Butyl Ketone* and possibly other solvents can damage the nervous system.

WORKPLACE CONTROLS AND PRACTICES

Unless a less toxic chemical can be substituted for a hazardous substance, **ENGINEERING CONTROLS** are the most effective way of reducing exposure. The best protection is to enclose operations and/or provide local exhaust ventilation at the site of chemical release. Isolating operations can also reduce exposure. Using respirators or protective equipment is less effective than the controls mentioned above, but is sometimes necessary.

In evaluating the controls present in your workplace, consider: (1) how hazardous the substance is, (2) how much of the substance is released into the workplace and (3) whether harmful skin or eye contact could occur. Special controls should be in place for highly toxic chemicals or when significant skin, eye, or breathing exposures are possible.

In addition, the following controls are recommended:

* Where possible, automatically pump liquid **Methyl Ethyl Ketone** from drums or other storage containers to process containers.
* Specific engineering controls are recommended for this chemical by NIOSH. Refer to the NIOSH criteria document: *Ketones #78-173*.

Good **WORK PRACTICES** can help to reduce hazardous exposures. The following work practices are recommended:

* Workers whose clothing has been contaminated by **Methyl Ethyl Ketone** should change into clean clothing promptly.
* Contaminated work clothes should be laundered by individuals who have been informed of the hazards of exposure to **Methyl Ethyl Ketone**.
* Eye wash fountains should be provided in the immediate work area for emergency use.
* If there is the possibility of skin exposure, emergency shower facilities should be provided.
* On skin contact with **Methyl Ethyl Ketone**, immediately wash or shower to remove the chemical. At the end of the workshift, wash any areas of the body that may have contacted **Methyl Ethyl Ketone**, whether or not known skin contact has occurred.
* Do not eat, smoke, or drink where **Methyl Ethyl Ketone** is handled, processed, or stored, since the chemical can be swallowed. Wash hands carefully before eating, drinking, smoking or using the toilet.

PERSONAL PROTECTIVE EQUIPMENT

WORKPLACE CONTROLS ARE BETTER THAN PERSONAL PROTECTIVE EQUIPMENT. However, for some jobs (such as outside work, confined space entry, jobs done only once in a while, or jobs done while workplace controls are being installed), personal protective equipment may be appropriate.

The following recommendations are only guidelines and may not apply to every situation.

Clothing

* Avoid skin contact with **Methyl Ethyl Ketone**. Wear solvent-resistant gloves and clothing. Safety equipment suppliers/manufacturers can provide recommendations on the most protective glove/clothing material for your operation.
* All protective clothing (suits, gloves, footwear, headgear) should be clean, available each day, and put on before work.
* ACGIH recommends the use of *Butyl Rubber* materials in protective clothing.

Eye Protection

* Wear splash-proof chemical goggles and face shield when working with liquid, unless full facepiece respiratory protection is worn.

Respiratory Protection

IMPROPER USE OF RESPIRATORS IS DANGEROUS. Such equipment should only be used if the employer has a written program that takes into account workplace conditions, requirements for worker training, respirator fit testing and medical exams, as described in OSHA 1910.134.

* Where the potential exists for exposures over **200 ppm**, use a MSHA/NIOSH approved full facepiece respirator with an organic vapor cartridge/canister. More protection is provided by a full facepiece respirator than by a half-mask respirator, and even greater protection is provided by a powered-air purifying respirator.
* If while wearing a filter, cartridge or canister respirator, you can smell, taste, or otherwise detect **Methyl Ethyl Ketone**, or in the case of a full facepiece respirator you experience eye irritation, leave the area immediately. Check to make sure the respirator-to-face seal is still good. If it is, replace the filter, cartridge, or canister. If the seal is no longer good, you may need a new respirator.
* Be sure to consider all potential exposures in your workplace. You may need a combination of filters, prefilters, cartridges, or canisters to protect against different forms of a chemical (such as vapor and mist) or against a mixture of chemicals.
* Where the potential for high exposures exists, use a MSHA/NIOSH approved supplied-air respirator with a full facepiece operated in a pressure-demand or other positive-pressure mode. For increased protection use in combination with an auxiliary self-contained breathing apparatus operated in a pressure-demand or other positive-pressure mode.
* Exposure to **3,000 ppm** is immediately dangerous to life and health. If the possibility of exposure above **3,000 ppm** exists, use a MSHA/NIOSH approved self-contained breathing apparatus with a full facepiece operated in a pressure-demand or other positive-pressure mode.

HANDLING AND STORAGE

* Prior to working with **Methyl Ethyl Ketone** you should be trained on its proper handling and storage.
* **Methyl Ethyl Ketone** must be stored to avoid contact with STRONG OXIDIZERS (such as CHLORINE, BROMINE and FLUORINE) since violent reactions occur.
* Store in tightly closed containers in a cool, well-ventilated area away from HEAT, SPARKS or FLAME.

* Sources of ignition, such as smoking and open flames, are prohibited where **Methyl Ethyl Ketone** is used, handled, or stored in a manner that could create a potential fire or explosion hazard.
* Metal containers involving the transfer of **Methyl Ethyl Ketone** should be grounded and bonded. Drums must be equipped with self-closing valves, pressure vacuum bungs, and flame arresters.
* Use only non-sparking tools and equipment, especially when opening and closing containers of **Methyl Ethyl Ketone**.

QUESTIONS AND ANSWERS

Q: If I have acute health effects, will I later get chronic health effects?
A: Not always. Most chronic (long-term) effects result from repeated exposures to a chemical.

Q: Can I get long-term effects without ever having short-term effects?
A: Yes, because long-term effects can occur from repeated exposures to a chemical at levels not high enough to make you immediately sick.

Q: What are my chances of getting sick when I have been exposed to chemicals?
A: The likelihood of becoming sick from chemicals is increased as the amount of exposure increases. This is determined by the length of time and the amount of material to which someone is exposed.

Q: When are higher exposures more likely?
A: Conditions which increase risk of exposure include physical and mechanical processes (heating, pouring, spraying, spills and evaporation from large surface areas such as open containers), and "confined space" exposures (working inside vats, reactors, boilers, small rooms, etc.).

Q: Is the risk of getting sick higher for workers than for community residents?
A: Yes. Exposures in the community, except possibly in cases of fires or spills, are usually much lower than those found in the workplace. However, people in the community may be exposed to contaminated water as well as to chemicals in the air over long periods. Because of this, and because of exposure of children or people who are already ill, community exposures may cause health problems.

Q: Can men as well as women be affected by chemicals that cause reproductive system damage?
A: Yes. Some chemicals reduce potency or fertility in both men and women. Some damage sperm and eggs, possibly leading to birth defects.

Q: Who is at the greatest risk from reproductive hazards?
A: Pregnant women are at greatest risk from chemicals that harm the developing fetus. However, chemicals may affect the ability to have children, so both men and women of childbearing age are at high risk.

Q: Should I be concerned if a chemical is a teratogen in animals?
A: Yes. Although some chemicals may affect humans differently than they affect animals, damage to animals suggests that similar damage can occur in humans.

The following information is available from:

New Jersey Department of Health and
Senior Services
Occupational Disease and Injury Services
Trenton, NJ 08625-0360
(609) 984-1863

Industrial Hygiene Information

Industrial hygienists are available to answer your questions regarding the control of chemical exposures using exhaust ventilation, special work practices, good housekeeping, good hygiene practices, and personal protective equipment including respirators. In addition, they can help to interpret the results of industrial hygiene survey data.

Medical Evaluation

If you think you are becoming sick because of exposure to chemicals at your workplace, you may call a Department of Health and Senior Services physician who can help you find the services you need.

Public Presentations

Presentations and educational programs on occupational health or the Right to Know Act can be organized for labor unions, trade associations and other groups.

Right to Know Information Resources

The Right to Know Infoline (609) 984-2202 can answer questions about the identity and potential health effects of chemicals, list of educational materials in occupational health, references used to prepare the Fact Sheets, preparation of the Right to Know survey, education and training programs, labeling requirements, and general information regarding the Right to Know Act. Violations of the law should be reported to (609) 984-2202.

DEFINITIONS

ACGIH is the American Conference of Governmental Industrial Hygienists. It recommends upper limits (called TLVs) for exposure to workplace chemicals.

A **carcinogen** is a substance that causes cancer.

The **CAS number** is assigned by the Chemical Abstracts Service to identify a specific chemical.

A **combustible** substance is a solid, liquid or gas that will burn.

A **corrosive** substance is a gas, liquid or solid that causes irreversible damage to human tissue or containers.

DEP is the New Jersey Department of Environmental Protection.

DOT is the Department of Transportation, the federal agency that regulates the transportation of chemicals.

EPA is the Environmental Protection Agency, the federal agency responsible for regulating environmental hazards.

A **fetus** is an unborn human or animal.

A **flammable** substance is a solid, liquid, vapor or gas that will ignite easily and burn rapidly.

The **flash point** is the temperature at which a liquid or solid gives off vapor that can form a flammable mixture with air.

HHAG is the Human Health Assessment Group of the federal EPA.

IARC is the International Agency for Research on Cancer, a scientific group that classifies chemicals according to their cancer-causing potential.

A **miscible** substance is a liquid or gas that will evenly dissolve in another.

mg/m^3 means milligrams of a chemical in a cubic meter of air. It is a measure of concentration (weight/volume).

MSHA is the Mine Safety and Health Administration, the federal agency that regulates mining. It also evaluates and approves respirators.

A **mutagen** is a substance that causes mutations. A **mutation** is a change in the genetic material in a body cell. Mutations can lead to birth defects, miscarriages, or cancer.

NAERG is the North American Emergency Response Guidebook. It was jointly developed by Transport Canada, the United States Department of Transportation and the Secretariat of Communications and Transportation of Mexico. It is a guide for first responders to quickly identify the specific or generic hazards of material involved in a transportation incident, and to protect themselves and the general public during the initial response phase of the incident.

NCI is the National Cancer Institute, a federal agency that determines the cancer-causing potential of chemicals.

NFPA is the National Fire Protection Association. It classifies substances according to their fire and explosion hazard.

NIOSH is the National Institute for Occupational Safety and Health. It tests equipment, evaluates and approves respirators, conducts studies of workplace hazards, and proposes standards to OSHA.

NTP is the National Toxicology Program which tests chemicals and reviews evidence for cancer.

OSHA is the Occupational Safety and Health Administration, which adopts and enforces health and safety standards.

PEOSHA is the Public Employees Occupational Safety and Health Act, a state law which sets PELs for New Jersey public employees.

ppm means parts of a substance per million parts of air. It is a measure of concentration by volume in air.

A **reactive** substance is a solid, liquid or gas that releases energy under certain conditions.

A **teratogen** is a substance that causes birth defects by damaging the fetus.

TLV is the Threshold Limit Value, the workplace exposure limit recommended by ACGIH.

The **vapor pressure** is a measure of how readily a liquid or a solid mixes with air at its surface. A higher vapor pressure indicates a higher concentration of the substance in air and therefore increases the likelihood of breathing it in.

>>>>>>>>>>>>>>>>> EMERGENCY INFORMATION <<<<<<<<<<<<<<<<<

Common Name: **METHYL ETHYL KETONE**
DOT Number: **UN 1193**
NAERG Code: **127**
CAS Number: **78-93-3**

Hazard rating	NJ DOH	NFPA
FLAMMABILITY	-	3
REACTIVITY	-	0
POISONOUS GASES ARE PRODUCED IN FIRE CONTAINERS MAY EXPLODE IN FIRE		

Hazard Rating Key: 0=minimal; 1=slight; 2=moderate; 3=serious; 4=severe

FIRE HAZARDS

* **Methyl Ethyl Ketone** is a FLAMMABLE LIQUID.
* Use dry chemical, CO_2, or alcohol foam extinguishers. Water should be used to keep fire-exposed containers cool.
* POISONOUS GASES ARE PRODUCED IN FIRE.
* Vapors may travel to a source of ignition and flash back.
* CONTAINERS MAY EXPLODE IN FIRE.
* If employees are expected to fight fires, they must be trained and equipped as stated in OSHA 1910.156.

SPILLS AND EMERGENCIES

If **Methyl Ethyl Ketone** is spilled or leaked, take the following steps:

* Evacuate and isolate the area of the spill or leak, and restrict persons not wearing protective equipment from area of spill or leak until clean-up is complete.
* Remove all ignition sources.
* Ventilate area of spill or leak.
* Absorb liquids in vermiculite, dry sand, earth, or a similar material and deposit in sealed containers.
* Keep **Methyl Ethyl Ketone** out of a confined space, such as a sewer, because of the possibility of an explosion, unless the sewer is designed to prevent the build-up of explosive concentrations.
* It may be necessary to contain and dispose of **Methyl Ethyl Ketone** as a HAZARDOUS WASTE. Contact your Department of Environmental Protection (DEP) or your regional office of the federal Environmental Protection Agency (EPA) for specific recommendations.
* If employees are required to clean-up spills, they must be properly trained and equipped. OSHA 1910.120(q) may be applicable.

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FOR LARGE SPILLS AND FIRES immediately call your fire department. You can request emergency information from the following:

CHEMTREC: (800) 424-9300
NJDEP HOTLINE: (609) 292-7172

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HANDLING AND STORAGE (See page 3)

FIRST AID

In NJ, POISON INFORMATION 1-800-962-1253

Eye Contact

* Immediately flush with large amounts of water for at least 15 minutes, occasionally lifting upper and lower lids. Seek medical attention.

Skin Contact

* Quickly remove contaminated clothing. Immediately wash area with large amounts of water. Seek medical attention.

Breathing

* Remove the person from exposure.
* Begin rescue breathing if breathing has stopped and CPR if heart action has stopped.
* Transfer promptly to a medical facility.

PHYSICAL DATA

Vapor Pressure: 70.6 mm Hg at 68^{O}F (20^{O}C)
Flash Point: 21^{O}F (-6.1^{O}C)
Water Solubility: Soluble

OTHER COMMONLY USED NAMES

Chemical Name:

2-Butanone

Other Names:

MEK; Ethyl Methyl Ketone; Butanone

Not intended to be copied and sold for commercial purposes.

NEW JERSEY DEPARTMENT OF HEALTH AND
SENIOR SERVICES
Right to Know Program
PO Box 368, Trenton, NJ 08625-0368
(609) 984-2202

Web Sites

that offer searchable chemical databases, recommended by Scorecard

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If you want more detailed information about a chemical than Scorecard provides, there are several on-line and library resources Scorecard recommends for further research.

ON-LINE CHEMICAL DATABASES

CambridgeSoft Chemfinder
http://chemfinder.camsoft.com/

Search

Chemfinder gives basic physico-chemical data and molecular structures for chemicals, and provides links to international data sources addressing specific chemicals.

Hazardous Substances Data Bank
http://toxnet.nlm.nih.gov/

Search

HSDB focuses on the toxicology of potentially hazardous chemicals, and includes peer-reviewed information on human exposure, industrial hygiene, emergency handling procedures, environmental fate, and regulatory requirements.

University of Akron Hazardous Chemicals Database
http://ull.chemistry.uakron.edu/erd/

Search

The Hazardous Chemicals Database provides physical data on chemicals and links to Department of Transportation safety guides that are valuable for emergency response.

BIBLIOGRAPHIC RESOURCES ON CHEMICAL TOXICITY

Scorecard provides qualitative summaries of the health hazards posed by a chemical (e.g., it is a suspected neurotoxicant), but not direct access to supporting toxicological data. These scientific studies are abstracted in several toxicity databases, which are available in libraries, from commercial vendors, and sometimes on-line. The major toxicity databases include:

The Registry of Toxic Effects of Chemicals Substances (RTECS)
RTECS is a database of toxicological information compiled by the National Institute for Occupational Safety and Health. It contains summary information about the types of health effects chemicals can cause and the concentrations at which toxicity is known to occur. It is available from several commercial vendors at http://www.cdc.gov/niosh/rtecs.html, and can often be found at major public or university libraries.

TOXLINE
Free access to the National Library of Medicine's toxicology-specific database of abstracts, reference journal articles, and reports is available at http://www.medscape.com/misc/FormToxlineInfLive.html

MEDLINE

Free access to the National Library of Medicine's MEDLINE database of more than 9 million references to articles published in 3800 biomedical journals is available at http://www.nlm.nih.gov/databases/freemedl.html. Two Web-based products, PubMed and Internet Grateful Med, provide this access. Medline can also be accessed at http://www.medscape.com/misc/FormMedlineInfLive.html

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TOLUENE (108-88-3)

summary from the About the Chemicals section of Scorecard

- **Human Health Hazards**

		Reference(s)
Recognized:	Developmental Toxicant	P65
Suspected:	Cardiovascular or Blood Toxicant	EPA-HEN KLAA RTECS
	Gastrointestinal or Liver Toxicant	RTECS
	Immunotoxicant	IPCS
	Kidney Toxicant	KLAA RTECS STAC
	Neurotoxicant	DAN EPA-HEN FELD OEHHA-2000 OEHHA-AREL RTECS
	Reproductive Toxicant	EPA-SARA
	Respiratory Toxicant	EPA-HEN LU OEHHA-2000 OEHHA-AREL
	Skin or Sense Organ Toxicant	EPA-HEN OEHHA-AREL

- **Hazard Rankings**

  More hazardous than most chemicals in 3 out of 10 ranking systems.

- **Chemical Use Profile**

  This is a high volume chemical with production exceeding 1 million pounds annually in the U.S.
  Used in at least 13 industries.
  Used in consumer products, building materials or furnishings that contribute to indoor air pollution.

- **Profile of Environmental Release and Waste Generation**

  For a list of the geographic areas, facilities, or industrial sectors which report the largest releases or transfers of this chemical to the Toxics Release Inventory, select what you want:

  - Rank States
  - Rank Counties
  - Rank Zip Codes
  - Rank Facilities
  - Rank Industrial Sectors

- **Regulatory Coverage**

  On at least 7 federal regulatory lists.

- **Basic Testing to Identify Chemical Hazards**

  Eight basic tests to identify chemical hazards have been conducted and are publicly

available for this chemical.

- **Information Needed for Safety Assessment**

  Possesses all the national data required for safety assessment.
  Scorecard has risk assessment data for this chemical.

- **Links**

  Additional information about this chemical may be available elsewhere in Scorecard.

  Other web sites specific to this chemical:

  - Agency for Toxic Substances and Disease Registry Public Health Statement
  - Agency for Toxic Substances and Disease Registry ToxFAQ
  - CalEPA Air Resources Board Toxic Air Contaminant Summary
  - EPA Health Effects Notebook for Hazardous Air Pollutants
  - EPA Integrated Risk Information System Report
  - EPA Office of Ground Water and Drinking Water Contaminant Fact Sheet
  - EPA Office of Pollution Prevention and Toxics Chemical Fact Sheet
  - EPA Office of Pollution Prevention and Toxics Chemical Fact Summary
  - Environmental Writer Chemical Backgrounder
  - IPCS International Chemical Safety Card
  - International Toxicity Estimates for Risk (ITER) from the Toxicology Excellence for Risk Assessment
  - National Toxicology Program Health and Safety Information Sheet

  If none of these sources meet your needs, you can try searching some other chemical database Web sites.

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Immunotoxicity Definitions

from the Health Effects section of Scorecard

Immunotoxicity is defined as adverse effects on the functioning of the immune system that result from exposure to chemical substances. Altered immune function may lead to the increased incidence or severity of infectious diseases or cancer, since the immune system's ability to respond adequately to invading agents is suppressed. Identifying immunotoxicants is difficult because chemicals can cause a wide variety of complicated effects on immune function. Observations in humans and studies in rodents have clearly demonstrated that a number of environmental and industrial chemicals can adversely affect the immune system. Exposure to asbestos, benzene, and halogenated aromatic hydrocarbons such as polybrominated biphenyls (PBBs), polychlorinated biphenyls (PCBs), and dioxins (TCDD) can lead to immunosuppression in humans. Toxic agents can also cause autoimmune diseases, in which healthy tissue is attacked by an immune system that fails to differentiate self-antigens from foreign antigens. For example, the pesticide dieldrin induces an autoimmune response against red blood cells, resulting in hemolytic anemia.

Also considered to be immunotoxicants, allergens are compounds that stimulate the immune system and can cause hypersensitivity reactions or allergies. Many chemicals induce allergic reactions in humans and experimental animals, producing a variety of clinical manifestations, such as asthma, rhinitis, and anaphylaxis. The industrial chemical toluene diisocyanate (TDI) and metals such as nickel and beryllium are notable examples of allergenic agents.

For further general information on chemicals and immunotoxicity, see the following references:

Dean, J., M. Murray, and E. Ward. Toxic Responses of the Immune System. Chapter 9 in Casarett and Doull's Toxicology, edited by C. Klaassen, M. Amdur, and J. Doull. New York: Pergamon Press, 1996.

Holladay, S. D., and M. Luster. Chemically-Induced Alterations in the Developing Immune System: The Wildlife/Human Connection. Environmental Health Perspectives 104 (Supplement 4): 809- 814. 1996.

Krzystyniak, K. Approaches to the Evaluation of Chemical Induced Immunotoxicity. Environmental Health Perspectives 203(9): 17-23. 1995.

Luster, M. I. Immunotoxicology: Clinical Consequences. Toxicology and Industrial Health. 12(3): 533-535. 1996.

Luster, M. I., and G. Rosenthal. Chemical Agents and the Immune Response. Environmental Health Perspectives. 100: 219-236. 1993.

Office of Technology Assessment. Identifying and Controlling Immunotoxic Substances. Washington, D.C.: Government Printing Office, 1991.

Thomas, P. T. Pesticide-Induced Immunotoxicity: Are the Great Lakes at Risk? Environmental Health Perspectives. 103 (Supplement 9): 55-61. 1995.

More

- references used to compile the list of immunotoxicants
- list of immunotoxicants

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Immunotoxicity References

from the Health Effects section of Scorecard

There is no generally accepted source for an authoritative list of chemicals that are recognized to cause immunotoxicity.

EDF's list of suspect immunotoxicants is compiled from the following sources:

CAA-AQC: US Environmental Protection Agency, Office of Research and Development. Air Quality Criteria for Oxides of Nitrogen, Volume III Washington, DC. August 1993.

CAPCOA: California Environmental Protection Agency and California Air Pollution Control Officers Association. Air Toxics Hotspots Program Risk Assessment Guidance: Revised 1992 Risk Assessment Guidance and Draft Evaluation of Acute Non-Cancer Health Effects. Office of Environmental Health Hazard Assessment, CalEPA, Berkeley, CA. December 1994 and January 1995. http://www.oehha.org/air/hot_spots/index.html

EEC: European Economic Community. Sensitizing Substances in the EEC List of Dangerous Substances. Annex I to Council Directive 67/548/EEC.

EPA-HEN: US Environmental Protection Agency. Health Effects Notebook for Hazardous Air Pollutants. Review Draft. December 1994. http://www.epa.gov/ttn/uatw/hapindex.html

EPA-TRI: US Environmental Protection Agency. Addition of Certain Chemicals; Toxic Chemical Release Reporting; Community Right to Know. Proposed and Final Rules. 59 Federal Register 1788 (Jan 12, 1994); 59 Federal Register 61432 (November 30, 1994).

IPCS: International Programme of Chemical Safety Environmental Health Criteria 180. Principles and Methods for Assessing Direct Immunotoxicity Associated with Exposure to Chemicals. World Health Organization. Geneva, 1996. (Table 1: Examples of compounds that are immunotoxic for humans or rodents).

NAP: Nordic Council of Ministers (Nordic Allergy Project). Kriteriedokumenter fra nordisk allergiprojekt - vurdering af 50 kemiske stoffers evne til at forarsage allergi, en litteraturgennemgang. Nord 1991:51. Copenhagen, 1991.

NTP-I: National Toxicology Program. Summary Reports on Immunotoxicity. http://ntp-server.niehs.nih.gov/htdocs/pub- IT0.html

OEHHA-2000: Office of Environmental Health Hazard Assessment, California Environmental Protection Agency. Air Toxics Hot Spots Program Risk Assessment Guidelines, Part III. February, 2000 (http://www.oehha.ca.gov/air/chronic_rels/22RELS2k.html) and May, 2000 (http://www.oehha.ca.gov/air/chronic_rels/42kChREL.html)

OEHHA-99: Office of Environmental Health Hazard Assessment, California Environmental Protection Agency. Air Toxics Hot Spots Program Risk Assessment Guidelines, Part III, Draft Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels. June 1999 (http://www.oehha.ca.gov/air/chronic_rels/RAGSII.html) and October, 1999

(http://www.oehha.ca.gov/air/chronic_rels/RAGSp3draft.html).

OEHHA-97: Office of Environmental Health Hazard Assessment, California Environmental Protection Agency. Draft Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels. October 1997. http://www.oehha.org/air/chronic_rels/GETRELS.html

RTECS: National Institute for Occupational Safety and Health's Registry of Toxic Effects of Chemical Substances. See EDF's Suspect Hazard Identification documentation.

SNCI: Swedish National Chemicals Inspectorate. Labelling of chemical products, Swedish regulations and general advice with regard to the classification and labelling of chemical products hazardous to health, flammables and explosives. List of Allergenic Substances. National Chemicals Inspectorate, Solna, Sweden. 1987, 1990-1992.

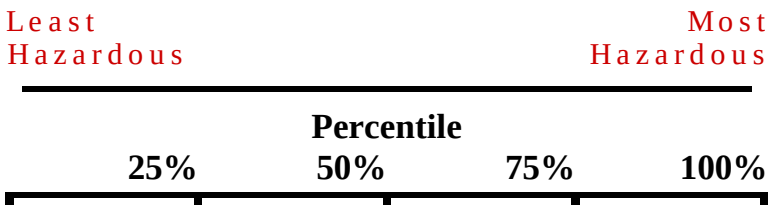
More

- definition of immunotoxicity
- list of immunotoxicants

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Hazard Rankings

for TOLUENE (108-88-3) from Scorecard



Human Health Rankings

Toxicity only

- Ingestion Toxicity Weight (RSEI)
- Inhalation Toxicity Weight (RSEI)
- Human Health Effects Score (UTN)

Toxicity and exposure potential

- Noncancer Risk Score - Air Releases (EDF)
- Noncancer Risk Score - Water Releases (EDF)
- Worker Exposure Hazard Score (IRCH)

Ecological Health Rankings

Toxicity only

- Ecological Effects Score (UTN)

Toxicity and persistence

- Environmental Hazard Value Score (IRCH)

Integrated Environmental Rankings

Combined human and ecological scores

- Total Hazard Value Score (IRCH)
- Total Hazard Value Score (UTN)

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Industrial Uses

for TOLUENE (108-88-3) from Scorecard

This is a high volume chemical with production exceeding 1 million pounds annually in the U.S.

Which Industries Use This Chemical?	How is the Chemical Used in This Industry?
Adhesives Manufacture	Carpet adhesive solvents
Electroplating	Electroplating - Cold-cleaning Solvents
Electroplating	Electroplating - Vapor Degreasing Solvents
Laboratory Chemicals	Solvents - Dilution
Laboratory Chemicals	Solvents - Extraction
Machinery Mfg and Repair	Solvents - Machinery Manufacture and Repair
Metal Degreasing	Solvents - Metal Degreasing
Paint Manufacture	Hydrocarbon Solvents
Paint Stripping	Solvents - Paint Stripping
Paper Coating	Solvents
Pesticide Mfg (Insecticides)	Solvents - Insecticide Manufacture
Pharmaceuticals Mfg	Solvents - Pharmaceuticals
Printing	Solvents for Flexography
Printing	Solvents for Gravure Printing
Rubber Manufacture	Solvents - Rubber Manufacture
Wood Stains and Varnishes	Varnish Solvents

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Consumer Products

that contain TOLUENE (108-88-3) from Scorecard

What kinds of consumer products may contain this chemical?

- Adhesive films, all types, incl pressure sensitive
- Aerosol paint concentrates
- Architectural coatings
- Auto, other transportation, and machinery refinish paints incl primers
- Automobile body polish and cleaners
- Floor polish
- Furniture polish and cleaners
- General performance sealants (PVAC, butyl, vinyl, etc.)
- Gravure inks
- Ground/traffic marking coatings
- Household hard surface cleaners (aerosol)
- Household hard surface cleaners (liquid)
- Industrial interior coatings
- Industrial particleboard (furniture, fixtures, cabinets, etc.)
- Laundry starch preparations
- Leather dressings and finishes (excl shoe polish)
- Loose mineral wool fiber (blowing and pouring)
- Lubricating oils
- Misc. use aromatics
- Miscellaneous paint-related products
- Moisturizing creams
- Nail enamels and polishes
- Non-wood upholstered office side and arm chairs
- Nonstructural caulking compounds and sealants
- Other art materials incl clay, water & tempera colors, finger paint, etc.
- Other automotive chemicals
- Other gravure inks
- Other industrial chemical specialty products
- Other laundry aids, icluding ironing aids and dry cleaning spotting pre
- Other manicuring preparations
- Other miscellaneous allied paint products, including brush cleaners
- Other specialty cleaning and sanitation products

- Packaging inks: solvent types
- Packaging inks: solvent types
- Paint and varnish removers
- Paint thinners
- Paints and allied products
- Phenolic and phenolic derivative adhesives
- Polyvinyl acetate (latex type) adhesives
- Publication inks: solvent types
- Scatter rugs, bathmats, and sets (rugs 6 x 9 ft and smaller)
- Sheet vinyl flooring
- Shoe polishes and cleaners
- Solvent thinned exterior stains incl shingle and shake
- Solvent thinned exterior undercoaters and primers
- Solvent thinned interior clear finishes
- Solvent thinned interior stains
- Solvent thinned interior undercoaters and primers
- Specialty performance sealants
- Surfactants, finishing agents, and assistants
- Synthetic resin and rubber adhesives
- Thick line coloring pens and markers
- Urethane adhesives
- Wall coverings
- Waterproofing compounds
- Wood office furniture
- Wood office secretarial chairs
- Wood office work surfaces (modular systems)

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States with Reported Total Environmental Releases

of TOLUENE (108-88-3) from the About The Chemicals section of Scorecard

---

Ranked by (select your ranking criteria)

Total environmental releases Go (explain)

1. TENNESSEE: 7,614,195 Pounds
2. INDIANA: 6,161,296 Pounds
3. MICHIGAN: 5,747,201 Pounds
4. TEXAS: 5,419,210 Pounds
5. NORTH CAROLINA: 5,338,563 Pounds
6. SOUTH CAROLINA: 5,278,595 Pounds
7. PENNSYLVANIA: 5,200,936 Pounds
8. ILLINOIS: 4,318,528 Pounds
9. VIRGINIA: 4,107,884 Pounds
10. MISSISSIPPI: 3,698,359 Pounds
11. OHIO: 3,507,318 Pounds
12. KENTUCKY: 3,281,146 Pounds
13. LOUISIANA: 3,216,232 Pounds
14. NEW YORK: 3,204,480 Pounds
15. GEORGIA: 2,814,093 Pounds
16. ALABAMA: 2,790,959 Pounds
17. WISCONSIN: 2,291,662 Pounds
18. ARKANSAS: 2,207,434 Pounds
19. MINNESOTA: 1,952,084 Pounds
20. IOWA: 1,807,958 Pounds
21. MISSOURI: 1,674,310 Pounds
22. MASSACHUSETTS: 1,649,360 Pounds
23. FLORIDA: 1,545,622 Pounds
24. KANSAS: 1,524,330 Pounds
25. OKLAHOMA: 1,350,073 Pounds
26. CALIFORNIA: 1,212,287 Pounds
27. NEW JERSEY: 1,172,525 Pounds
28. PUERTO RICO: 1,072,289 Pounds

29. WASHINGTON: 909,806 Pounds
30. WEST VIRGINIA: 797,998 Pounds
31. NEBRASKA: 677,803 Pounds
32. CONNECTICUT: 677,072 Pounds
33. OREGON: 619,953 Pounds
34. NEVADA: 584,692 Pounds
35. RHODE ISLAND: 522,730 Pounds
36. MARYLAND: 390,928 Pounds
37. UTAH: 342,858 Pounds
38. IDAHO: 341,520 Pounds
39. NEW MEXICO: 303,008 Pounds
40. COLORADO: 289,033 Pounds
41. MAINE: 267,017 Pounds
42. SOUTH DAKOTA: 184,172 Pounds
43. NEW HAMPSHIRE: 177,622 Pounds
44. NORTH DAKOTA: 126,581 Pounds
45. WYOMING: 106,394 Pounds
46. MONTANA: 101,504 Pounds
47. ARIZONA: 79,160 Pounds
48. ALASKA: 77,765 Pounds
49. VIRGIN ISLANDS: 53,951 Pounds
50. VERMONT: 42,797 Pounds
51. DELAWARE: 39,190 Pounds
52. HAWAII: 29,724 Pounds
53. GUAM: 7,296 Pounds
54. NORTHERN MARIANA ISLANDS: 2,071 Pounds
55. AMERICAN SAMOA: 1,695 Pounds

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Counties with Reported Total Environmental Releases

of TOLUENE (108-88-3) from the About The Chemicals section of Scorecard

---

Ranked by (select your ranking criteria)

Total environmental releases

in

Entire United States Go (explain)

1. RICHLAND, SC: 3,026,051 pounds
2. DICKSON, TN: 2,127,920 pounds
3. CATAWBA, NC: 2,071,363 pounds
4. ST. CLAIR, MI: 1,761,731 pounds
5. ALCORN, MS: 1,565,860 pounds
6. SIMPSON, KY: 1,138,720 pounds
7. SPARTANBURG, SC: 1,128,338 pounds
8. SHELBY, TN: 1,053,274 pounds
9. SUMNER, TN: 1,015,969 pounds
10. JEFFERSON, TX: 1,004,466 pounds
11. HENRICO, VA: 982,475 pounds
12. KOSCIUSKO, IN: 969,333 pounds
13. BUCKS, PA: 954,970 pounds
14. KENT, MI: 946,938 pounds
15. CHESTER, PA: 878,936 pounds
16. HARRIS, TX: 864,813 pounds
17. JEFFERSON, KY: 864,251 pounds
18. DALLAS, TX: 858,690 pounds
19. ERIE, NY: 819,397 pounds
20. LANCASTER, PA: 814,053 pounds
21. COLES, IL: 794,779 pounds
22. COOK, IL: 733,103 pounds
23. COLUMBIA, GA: 705,747 pounds
24. BAYAMO'N, PR: 695,195 pounds
25. FORREST, MS: 653,777 pounds

26. MARION, IL: 648,067 pounds
27. CALCASIEU, LA: 641,248 pounds
28. OSAGE, OK: 628,106 pounds
29. OGLE, IL: 618,258 pounds
30. ASCENSION, LA: 617,606 pounds
31. LYNCHBURG (CITY), VA: 611,057 pounds
32. CALDWELL, NC: 598,569 pounds
33. IBERVILLE, LA: 592,307 pounds
34. SEBASTIAN, AR: 580,064 pounds
35. ELKHART, IN: 575,721 pounds
36. LAKE, IN: 574,805 pounds
37. HENRY, VA: 574,785 pounds
38. BRISTOL, MA: 571,347 pounds
39. NORTHUMBERLAND, PA: 562,178 pounds
40. WASHOE, NV: 555,859 pounds
41. DYER, TN: 523,298 pounds
42. LANCASTER, NE: 508,559 pounds
43. DADE, FL: 506,875 pounds
44. WAYNE, MI: 498,203 pounds
45. SEDGWICK, KS: 494,308 pounds
46. SEMINOLE, FL: 490,640 pounds
47. SUMTER, GA: 479,031 pounds
48. HAWKINS, TN: 473,012 pounds
49. PROVIDENCE, RI: 457,129 pounds
50. JOHNSON, IN: 451,860 pounds
51. SANTA CLARA, CA: 442,396 pounds
52. ORANGE, NY: 409,780 pounds
53. ST. CHARLES, LA: 403,718 pounds
54. WINSTON, AL: 401,547 pounds
55. RAMSEY, MN: 398,877 pounds
56. LOWNDES, MS: 398,612 pounds
57. WINNEBAGO, WI: 394,157 pounds
58. WAYNE, NY: 391,189 pounds

59. LOS ANGELES, CA: 384,496 pounds
60. POLK, IA: 384,125 pounds
61. MIDDLESEX, NJ: 379,274 pounds
62. HENNEPIN, MN: 373,444 pounds
63. MIDDLESEX, MA: 368,806 pounds
64. WASHINGTON, AL: 359,990 pounds
65. GARLAND, AR: 358,635 pounds
66. MARION, IA: 356,471 pounds
67. JEFFERSON, AL: 349,642 pounds
68. KING, WA: 343,373 pounds
69. COSHOCTON, OH: 342,186 pounds
70. LAUDERDALE, MS: 341,944 pounds
71. GIBSON, TN: 337,690 pounds
72. PHILADELPHIA, PA: 328,412 pounds
73. ST. LOUIS, MO: 317,853 pounds
74. PAYETTE, ID: 316,964 pounds
75. TULSA, OK: 312,828 pounds
76. POSEY, IN: 309,540 pounds
77. CHATHAM, GA: 307,377 pounds
78. OTTAWA, MI: 303,214 pounds
79. NEW HAVEN, CT: 301,595 pounds
80. ST. JOSEPH, MI: 299,987 pounds
81. ALLEN, OH: 289,513 pounds
82. LAKE, OH: 286,483 pounds
83. NUECES, TX: 285,355 pounds
84. WASHINGTON, MN: 283,992 pounds
85. CULLMAN, AL: 282,795 pounds
86. MIDLAND, MI: 278,959 pounds
87. RANDOLPH, IN: 278,260 pounds
88. SCOTT, KY: 271,650 pounds
89. LAUDERDALE, TN: 265,200 pounds
90. SULLIVAN, TN: 262,261 pounds
91. VENANGO, PA: 256,634 pounds

92. GALVESTON, TX: 256,550 pounds
93. MIAMI, OH: 256,205 pounds
94. COLUMBIA, WI: 251,493 pounds
95. RICHMOND, GA: 249,898 pounds
96. DAVIDSON, NC: 249,553 pounds
97. ROCKLAND, NY: 248,845 pounds
98. BUNCOMBE, NC: 243,447 pounds
99. HEMPSTEAD, AR: 238,887 pounds
100. MCLEOD, MN: 234,722 pounds

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Zip Codes with Reported Total Environmental Releases

of TOLUENE (108-88-3) from the About The Chemicals section of Scorecard

---

Ranked by (select your ranking criteria)

Total environmental releases

in

Entire United States Go (explain)

1. 29205 (SC): 3,016,064 pounds
2. 37055 (TN): 2,127,920 pounds
3. 28601 (NC): 1,859,574 pounds
4. 48040 (MI): 1,752,492 pounds
5. 38834 (MS): 1,565,860 pounds
6. 42134 (KY): 1,138,720 pounds
7. 37066 (TN): 1,015,969 pounds
8. 23228 (VA): 981,070 pounds
9. 46580 (IN): 886,548 pounds
10. 61938 (IL): 782,000 pounds
11. 40216 (KY): 779,038 pounds
12. 19310 (PA): 761,856 pounds
13. 14043 (NY): 742,742 pounds
14. 19007 (PA): 730,727 pounds
15. 30809 (GA): 705,747 pounds
16. 00959 (PR): 681,250 pounds
17. 77701 (TX): 681,246 pounds
18. 29301 (SC): 660,813 pounds
19. 39401 (MS): 653,777 pounds
20. 62881 (IL): 648,067 pounds
21. 38116 (TN): 628,515 pounds
22. 74002 (OK): 626,500 pounds
23. 70734 (LA): 617,606 pounds
24. 17601 (PA): 617,126 pounds
25. 61054 (IL): 613,206 pounds

26. 70601 (LA): 600,848 pounds
27. 24501 (VA): 594,925 pounds
28. 75244 (TX): 560,932 pounds
29. 89506 (NV): 555,859 pounds
30. 72908 (AR): 548,550 pounds
31. 70776 (LA): 543,832 pounds
32. 38024 (TN): 523,298 pounds
33. 49512 (MI): 508,442 pounds
34. 02720 (MA): 496,260 pounds
35. 46394 (IN): 493,968 pounds
36. 32750 (FL): 490,640 pounds
37. 31709 (GA): 479,031 pounds
38. 37642 (TN): 470,272 pounds
39. 29307 (SC): 464,155 pounds
40. 33169 (FL): 462,100 pounds
41. 68504 (NE): 453,834 pounds
42. 46124 (IN): 451,860 pounds
43. 17857 (PA): 443,607 pounds
44. 95131 (CA): 440,741 pounds
45. 28633 (NC): 439,113 pounds
46. 10940 (NY): 404,094 pounds
47. 14522 (NY): 391,189 pounds
48. 02908 (RI): 378,567 pounds
49. 36553 (AL): 359,990 pounds
50. 71901 (AR): 358,635 pounds
51. 39703 (MS): 353,000 pounds
52. 54952 (WI): 342,477 pounds
53. 43812 (OH): 342,186 pounds
54. 39301 (MS): 341,944 pounds
55. 50138 (IA): 327,080 pounds
56. 50321 (IA): 319,027 pounds
57. 83619 (ID): 316,964 pounds
58. 47620 (IN): 309,540 pounds

59. 31415 (GA): 301,230 pounds
60. 49093 (MI): 299,603 pounds
61. 67210 (KS): 298,005 pounds
62. 77536 (TX): 283,418 pounds
63. 35055 (AL): 282,795 pounds
64. 40324 (KY): 271,650 pounds
65. 55144 (MN): 267,926 pounds
66. 38063 (TN): 265,200 pounds
67. 55016 (MN): 261,586 pounds
68. 44077 (OH): 258,598 pounds
69. 53925 (WI): 251,493 pounds
70. 37662 (TN): 251,161 pounds
71. 47355 (IN): 251,110 pounds
72. 30903 (GA): 245,782 pounds
73. 24055 (VA): 240,137 pounds
74. 71801 (AR): 238,887 pounds
75. 55350 (MN): 234,722 pounds
76. 46750 (IN): 234,368 pounds
77. 19134 (PA): 233,400 pounds
78. 38358 (TN): 233,152 pounds
79. 45373 (OH): 232,481 pounds
80. 35565 (AL): 232,107 pounds
81. 10962 (NY): 231,250 pounds
82. 49345 (MI): 230,246 pounds
83. 60501 (IL): 225,585 pounds
84. 71109 (LA): 224,231 pounds
85. 38108 (TN): 222,682 pounds
86. 01220 (MA): 217,334 pounds
87. 28704 (NC): 217,037 pounds
88. 07823 (NJ): 213,378 pounds
89. 46947 (IN): 212,611 pounds
90. 77590 (TX): 211,401 pounds
91. 46706 (IN): 211,129 pounds

92. 61537 (IL): 209,295 pounds
93. 76305 (TX): 208,200 pounds
94. 55414 (MN): 207,259 pounds
95. 21061 (MD): 200,993 pounds
96. 70066 (LA): 199,815 pounds
97. 13367 (NY): 195,892 pounds
98. 65265 (MO): 195,543 pounds
99. 22601 (VA): 194,071 pounds
100. 24089 (VA): 193,622 pounds

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Facilities with Reported Total Environmental Releases

of TOLUENE (108-88-3) from the About the Chemicals section of Scorecard

---

Ranked by (select your ranking criteria)

Total environmental releases

in

Entire United States

from

All reporting sectors

Go (explain)

1. INTERTAPE POLYMER GROUP ANCHOR, COLUMBIA, SC: 3,016,064 Pounds
2. QUEBECOR PRINTING INC., DICKSON, TN: 2,123,243 Pounds
3. SHURTAPE TECHS. INC., HICKORY TAPE PLANT, HICKORY, NC: 1,802,050 Pounds
4. INTERTAPE POLYMER GROUP, MARYSVILLE, MI: 1,752,492 Pounds
5. WORLD COLOR CORINTH DIV., CORINTH, MS: 1,430,720 Pounds
6. QUEBECOR PRINTING FRANKLIN, FRANKLIN, KY: 1,111,000 Pounds
7. QUEBECOR PRINTING RICHMOND INC., RICHMOND, VA: 981,070 Pounds
8. R. R. DONNELLEY & SONS CO., GALLATIN, TN: 954,600 Pounds
9. R. R. DONNELLEY & SONS CO., WARSAW, IN: 854,030 Pounds
10. R.R. DONNELLEY & SONS CO., MATTOON, IL: 782,000 Pounds
11. QUEBECOR PRINTING ATGLEN INC., ATGLEN, PA: 761,856 Pounds
12. QUEBECOR PRINTING BUFFALO INC., DEPEW, NY: 742,742 Pounds
13. 3M CO., BRISTOL, PA: 720,720 Pounds
14. WORLD COLOR, AUGUSTA DIV., EVANS, GA: 705,747 Pounds
15. AMERICAN SYNTHETIC RUBBER CORP., LOUISVILLE, KY: 685,000 Pounds
16. COATINGS INC. & CO., BAYAMON, PR: 680,386 Pounds
17. MOBIL OIL BEAUMONT REFY., BEAUMONT, TX: 678,000 Pounds
18. QUEBECOR PRINTING MEMPHIS L.P., MEMPHIS, TN: 628,515 Pounds
19. WORLD COLOR PRESS-SALEM DIVISION(SALEM GRAVURE), SALEM, IL: 627,600 Pounds
20. BAKER PETROLITE CORP., BARNSDALL, OK: 626,500 Pounds
21. R. R. DONNELLEY & SONS CO. LANCASTER EAST, LANCASTER, PA: 616,800 Pounds

22. QUEBECOR PRINTING MT. MORRIS INC., MOUNT MORRIS, IL: 613,206 Pounds
23. REEVES BROTHERS INC., SPARTANBURG, SC: 609,913 Pounds
24. CITGO PETROLEUM CORP., LAKE CHARLES, LA: 580,033 Pounds
25. QUEBECOR PRINTING DALLAS INC., FARMERS BRANCH, TX: 560,932 Pounds
26. R. R. DONNELLEY PRINTING CO., LYNCHBURG, VA: 558,000 Pounds
27. R.R. DONNELLEY & SONS CO.130130, RENO, NV: 554,000 Pounds
28. NOVARTIS CROP PROTECTION INC. ST. GABRIEL FACILITY, SAINT GABRIEL, LA: 537,444 Pounds
29. WHIRLPOOL CORP., FORT SMITH, AR: 530,750 Pounds
30. WORLD COLOR PRESS INC. DYERSBURG DIV., DYERSBURG, TN: 523,298 Pounds
31. GLOBE MFG. CO., FALL RIVER, MA: 496,260 Pounds
32. AMOCO OIL CO., WHITING REFY., WHITING, IN: 493,952 Pounds
33. DAVID M. CO., LONGWOOD, FL: 490,640 Pounds
34. HOLLISTON MILLS INC., CHURCH HILL, TN: 462,110 Pounds
35. NAILITE INTL. INC., MIAMI, FL: 462,100 Pounds
36. R. R. DONNELLEY & SONS CO., SPARTANBURG, SC: 458,001 Pounds
37. GOODYEAR TIRE & RUBBER CO., LINCOLN, NE: 453,834 Pounds
38. SONOCO FLEXIBLE PACKAGING, EDINBURGH, IN: 451,860 Pounds
39. RESILITE SPORTS PRODS. INC., NORTHUMBERLAND, PA: 443,607 Pounds
40. QUEBECOR PRINTING SAN JOSE INC., SAN JOSE, CA: 440,241 Pounds
41. TESA TAPE INC., MIDDLETOWN, NY: 404,094 Pounds
42. WOODGRAIN MILLWORK INC., AMERICUS, GA: 396,404 Pounds
43. GARLOCK INC., PALMYRA, NY: 391,189 Pounds
44. QUEBECOR PRINTING PROVIDENCE INC., PROVIDENCE, RI: 378,567 Pounds
45. CIBA SPECIALTY CHEMICALS CORP., MC INTOSH, AL: 359,990 Pounds
46. CHEM-FAB CORP., HOT SPRINGS, AR: 358,635 Pounds
47. GENCORP, COLUMBUS, MS: 353,000 Pounds
48. AMERICAN NATL. CAN CO. PPMW, MENASHA, WI: 342,477 Pounds
49. BORDEN CHEMICALS & PLASTICS OPERATING L.P., GEISMAR, LA: 334,846 Pounds
50. HERCULES INC., HATTIESBURG, MS: 331,797 Pounds

51. 3M, KNOXVILLE, IA: 327,080 Pounds
52. VENTURE GRAND RAPIDS LLC, GRAND RAPIDS, MI: 323,637 Pounds
53. ZEON CHEMICALS LP ., MISSISSIPPI PLANT, HATTIESBURG, MS: 321,980 Pounds
54. R. R. DONNELLEY PRINTING CO. L.P., DES MOINES, IA: 319,027 Pounds
55. WOODGRAIN MILLWORK INC., MILLWORK & PREFINISH DIVISIONS, FRUITLAND, ID: 316,964 Pounds
56. UNION CAMP CORP., SAVANNAH, GA: 301,230 Pounds
57. DAY INTL. INC., THREE RIVERS, MI: 299,603 Pounds
58. BOEING CO. - WICHITA DIV., WICHITA, KS: 298,005 Pounds
59. LUDLOW COATED PRODS., MERIDIAN, MS: 284,700 Pounds
60. GENERAL ELECTRIC PLASTICS CO., MOUNT VERNON, IN: 284,053 Pounds
61. TOYOTA MOTOR MFG. KENTUCKY INC., GEORGETOWN, KY: 271,650 Pounds
62. 3M, SAINT PAUL, MN: 267,926 Pounds
63. SHELL CHEMICAL CO. DEER PARK, DEER PARK, TX: 266,313 Pounds
64. 3M, COTTAGE GROVE CENTER, COTTAGE GROVE, MN: 261,586 Pounds
65. DCP-LOHJA INC., CULLMAN, AL: 251,500 Pounds
66. TENNESSEE EASTMAN DIV., KINGSPORT, TN: 251,161 Pounds
67. AMERICAN PACKAGING CORP., COLUMBUS, WI: 247,287 Pounds
68. DSM CHEMICALS N.A. INC., AUGUSTA, GA: 245,782 Pounds
69. BROYHILL FURNITURE IND. INC., MILLER HILL COMPLEX, LENOIR, NC: 241,341 Pounds
70. BRENTWOOD IND. INC., HOPE, AR: 238,754 Pounds
71. KEN-KOAT INC., HUNTINGTON, IN: 234,059 Pounds
72. 3M HUTCHINSON, HUTCHINSON, MN: 234,000 Pounds
73. ALDAN INDS. INC., PHILADELPHIA, PA: 233,400 Pounds
74. PAXAR CORP., ORANGEBURG, NY: 231,250 Pounds
75. PENNZOIL-QUAKER STATE CO. SHREVEPORT REFY., SHREVEPORT, LA: 224,231 Pounds
76. EXCELLO FABRIC FINISHERS INC., COSHOCTON, OH: 222,709 Pounds
77. 3M, TAPE MFG. DIV., BEDFORD PARK, IL: 221,797 Pounds
78. TESA TAPE INC., SPARTA, MI: 217,846 Pounds
79. POLYFIBRON TECHS. INC, ADAMS, MA: 217,334 Pounds
80. DAY INTL., ARDEN, NC: 217,037 Pounds

81. GREAT LAKES CHEMICAL CORP., MEMPHIS, TN: 216,100 Pounds
82. COOPER TIRE & RUBBER CO. ENGINEERED PRODS. DIV., AUBURN, IN: 211,129 Pounds
83. BF GOODRICH CO., HENRY, IL: 209,295 Pounds
84. ROCHE VITAMINS INC., BELVIDERE, NJ: 208,555 Pounds
85. TEXAS RECREATION CORP., WICHITA FALLS, TX: 208,200 Pounds
86. SR OF TENNESSEE, RIPLEY, TN: 208,050 Pounds
87. QUEBECOR PRINTING MEMPHIS INC., GLEN BURNIE, MD: 200,993 Pounds
88. WITCO CORP., POLYMER ADDITIVES DIV., KILLONA, LA: 199,815 Pounds
89. REXAM DSI, LOWVILLE, NY: 195,892 Pounds
90. TEVA PHARMACEUTICALS USA, MEXICO, MO: 195,543 Pounds
91. IMATION ENTERPRISES CORP., WHITE CITY, OR: 192,100 Pounds
92. JM CLIPPER CORP., NACOGDOCHES, TX: 191,000 Pounds
93. SLOSS IND. CORP., CHEMICAL PLANT, BIRMINGHAM, AL: 189,557 Pounds
94. AMOCO PETROLEUM PRODS. REFINING BUSINESS GROUP, TEXAS CITY, TX: 187,003 Pounds
95. COURTAULDS PERFORMANCE FILMS INC. PLANT II, FIELDALE, VA: 186,600 Pounds
96. QUAD/GRAPHICS INC., LOMIRA, WI: 185,720 Pounds
97. DOW CHEMICAL CO. - MIDLAND OPS., MIDLAND, MI: 184,030 Pounds
98. ALLIED-SIGNAL ASTOR CORP. MCKEAN PLANT, SMETHPORT, PA: 183,575 Pounds
99. MCLAREN ENGINES INC., LIVONIA, MI: 182,175 Pounds
100. UNIROYAL CHEMICAL CO. INC., GEISMAR, LA: 180,000 Pounds

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Industrial Sectors with Reported Total Environmental Releases

of TOLUENE (108-88-3) by Industrial Sector (2-digit SIC) from the About the Chemicals section of Scorecard

---

Ranked by (select your ranking criteria)

Total environmental releases

in

Entire United States Go (explain)

1. 27: Printing And Publishing : 18,076,596 pounds
2. 26: Paper And Allied Products : 15,073,499 pounds
3. 28: Chemicals And Allied Products : 13,588,452 pounds
4. 30: Rubber And Misc. Plastics Products : 10,528,491 pounds
5. 37: Transportation Equipment : 7,412,654 pounds
6. 29: Petroleum And Coal Products : 7,305,042 pounds
7. 25: Furniture And Fixtures : 5,525,401 pounds
8. 24: Lumber And Wood Products : 4,187,311 pounds
9. 34: Fabricated Metal Products : 4,002,999 pounds
10. 39: Miscellaneous Manufacturing Industries : 3,162,575 pounds
11. 36: Electronic & Other Electric Equipment : 2,055,364 pounds
12. 22: Textile Mill Products : 1,900,717 pounds
13. 35: Industrial Machinery And Equipment : 1,576,401 pounds
14. 33: Primary Metal Industries : 1,067,367 pounds
15. 51: Wholesale Trade--Nondurable Goods : 844,860 pounds
16. 32: Stone, Clay, And Glass Products : 715,377 pounds
17. 31: Leather And Leather Products : 596,385 pounds
18. 38: Instruments And Related Products : 408,584 pounds
19. 20: Food And Kindred Products : 318,705 pounds
20. 49: Electric, Gas, And Sanitary Services : 168,136 pounds
21. 23: Apparel And Other Textile Products : 107,126 pounds
22. NA: Not reported : 87,019 pounds
23. 21: Tobacco Products : 84,021 pounds
24. 97: National Security And Intl. Affairs : 52,804 pounds

25. 73: Business Services : 21,128 pounds
26. 13: Oil And Gas Extraction : 9,925 pounds
27. 44: Water Transportation : 3,198 pounds
28. 10: Metal Mining : 3,182 pounds
29. 87: Engineering & Management Services : 1,308 pounds
30. 42: Trucking And Warehousing : 294 pounds
31. 95: Environmental Quality And Housing : 5 pounds

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Regulatory Coverage

of TOLUENE (108-88-3) from Scorecard

Federal Regulatory Program Lists

- Air Contaminants (Occupational and Safety Health Act)
- Hazardous Air Pollutants (Clean Air Act)
- Hazardous Constituents (Resource Conservation and Recovery Act)
- Hazardous Substances (Superfund)
- Maximum Contaminant Levels (Safe Drinking Water Act)
- Priority Pollutants (Clean Water Act)
- Toxic Release Inventory Chemicals

California State Regulatory Program Lists

- California Air Toxics "Hot Spots" Chemicals (Assembly Bill 2588)
- California Toxic Air Contaminants (Assembly Bill 1807)
- Known Carcinogens and Reproductive Toxicants (California Proposition 65)
- Maximum Contaminant Levels (California Safe Drinking Water Act)

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Basic Testing to Identify Chemical Hazards

for TOLUENE (108-88-3) from Scorecard

The U.S. EPA conducted a comprehensive review of publicly available chemical testing data in 1997 to examine whether the basic information needed to identify chemical hazards is available for high production volume chemicals. EPA searched major chemical databases to determine if the following tests had been conducted on a chemical:

- Acute toxicity
- Chronic toxicity
- Neurotoxicity
- Developmental or reproductive toxicity
- Mutagenicity
- Carcinogenicity
- Ecotoxicity
- Environmental fate

Eight basic tests to identify chemical hazards have been conducted and are publicly available for this chemical.

More on the importance of basic toxicity testing

Reference

EPA. Chemical Hazard Data Availability Study: High Production Volume (HPV) Chemicals and SIDS Testing
Office of Pollution Prevention and Toxics, EPA,Washington, DC. 1998.

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Safety Assessment Data

for TOLUENE (108-88-3) from Scorecard

Are Risk Assessment Values Available?

Health Risk of Concern	Inhalation	Ingestion
Cancer	Not a recognized carcinogen	Not a recognized carcinogen
Noncancer	Yes	Yes

Are Exposure Data Available?

Type of Exposure	
Inhalation - ambient air	Monitoring data available in some states
Inhalation - indoor air	**No**
Ingestion	Yes

- See the data US EPA possesses for safety assessment.

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Scorecard Risk Characterization Data

for TOLUENE (108-88-3) from Scorecard

Risk Assessment Values or Standards

	Value	Units	Reference
Inhalation cancer risk value (potency)	Not a recognized or suspect carcinogen		
Inhalation noncancer risk value (reference concentration)	300	ug/m3	OEHHA2000-REL
National ambient air quality standard	Gap in regulatory coverage		
Ingestion cancer risk value (potency)	Not a recognized or suspect carcinogen		
Ingestion noncancer risk value (reference dose)	0.2	mg/kg-day	IRIS-HEAST
National water quality standard	1	mg/L	SDWA-MCL

See the data US EPA possesses for safety assessment.

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Chemical Classes

for TOLUENE (108-88-3) from Scorecard

Note that TOLUENE may be a member of the following classes:

- VOLATILE ORGANIC COMPOUNDS

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Agency for Toxic Substances and Disease Registry

Public Health Statement

Toluene

ATSDR Public Health Statement, December 1989

What is toluene?

Toluene is a clear, colorless liquid with a sweet smell. Toluene occurs naturally in crude oil and the tolu tree. It is produced from petroleum refining, as a by-product of styrene production, and as a by-product of coke-oven operations. Industry uses it in refining gasoline, chemical manufacturing, and manufacture of paints, lacquers, adhesives, rubber, and in some printing and leather tanning processes. Toluene is usually disposed of at hazardous waste sites as a used solvent (a substance used to dissolve other substances). Toluene doesn't usually stay in the environment; it readily breaks down in soil and evaporates from water.

How might I be exposed to toluene?

Humans may be exposed to toluene from many sources, including drinking water, food, air, workplaces, and consumer products. Exposure to toluene by humans occurs mostly through breathing the chemical in the workplace or during deliberate glue sniffing or solvent abuse. Toluene readily evaporates and can therefore be released to the air when toluene-containing products are used. Automobile exhaust can also be a significant source of toluene emissions to the air. Petrochemical workers, workers in the chemical industry, dye makers, and paint workers are at the greatest risk of exposure. Because toluene is a common solvent and is found in many consumer products, exposures may happen in the home and outdoors. Consumer products containing toluene include gasoline, nail polish, cosmetics, rubber cement, paint brush cleaners, stain removers, fabric dyes, inks, and adhesives. Smokers are exposed to toluene in cigarette smoke.

Exposure may happen at some hazardous waste sites. The U.S. Environmental Protection Agency (EPA) conducted a survey in 1988 and found toluene in groundwater, surface water, or soil at 29% of the hazardous waste sites surveyed. The average amounts of toluene at hazardous waste sites were 21 ppb (21 parts toluene per billion parts water) in groundwater and 7.5 ppb in surface water. The amount in soil was 77 ppb.

Federal and state surveys do not show toluene to be a widespread contaminant of drinking water supplies. Toluene was found in about 1% of the groundwater sources at amounts lower than 2 ppb. More was found in surface water supplies, but the surveys were not as complete as the groundwater surveys. Toluene levels in the air are typically lower than 1 ppm (one part toluene per million parts air) in nonindustrialized areas (cities and suburbs). Usual levels of toluene indoors are also lower than 1 ppm. Usual levels in food have not been reported.

How can toluene enter and leave my body?

Toluene can enter the body by passing through the skin, or when a person breathes its vapors, or eats or drinks contaminated food or water. Human exposure occurs mainly by breathing air containing toluene. Where a person lives, works, and travels and what a person eats affect daily exposure to toluene. Things such as age, sex, and health status affect what happens to toluene once it is in the body. After being taken into the body, most toluene leaves the body within 12 hours. It leaves the body unchanged in the exhaled air and also leaves the body as a breakdown product in the urine.

How can toluene affect my health?

The most important health concern for humans from either intentional or occupational exposure to toluene is its harmful effects on the nervous system. These effects of toluene depend on both the amount and length of exposure. Short-term exposure to moderate amounts of toluene, such as in elevated workplace exposures, can produce fatigue, confusion, general weakness, drunken-type actions, memory loss, nausea, and loss of appetite. These symptoms disappear when exposure is stopped.

Short-term exposure to high amounts of toluene results first in light-headedness and euphoria. This is followed by dizziness, sleepiness, unconsciousness, and, in some cases, death because the person cannot breathe prior to death. When exposure is stopped before death, these symptoms disappear. Long-term exposure to low and moderate amounts of toluene has caused slight effects on the kidneys in some people, but these people were also exposed to other solvents at the same time and it is difficult to tell which chemical may have caused the effects. Long-term exposure to high amounts of toluene by intentional abuse has been linked with permanent damage to the brain. Effects such as problems with speech, vision, and hearing; loss of muscle control; loss of memory and balance; and reduced scores on psychological tests have been reported. Researchers have seen possible effects on resistance to disease in persons exposed to moderate and high amounts of chemical mixtures that contained toluene. However, it is not possible to tell exactly which chemical in the mixture may have caused the effects.

In animals, as in humans, the main effect of toluene is on the nervous system. Exposure of animals to moderate and high amounts of toluene also produces slightly harmful effects on the liver, kidneys, and lungs. Several studies have shown that the development of unborn animals is affected or harmed when high levels of toluene are breathed in by pregnant animals. However, when pregnant animals were fed high amounts of toluene, the unborn animals did not show any developmental problems. It is not known if toluene will harm an unborn child when a pregnant woman drinks water or breathes in air containing toluene because studies in people are not complete enough to measure this effect. The National Toxicology Program (NTP) found that toluene did not cause cancer in a long-term study in rats and mice.

Is there a medical test to determine whether I have been exposed to toluene?

Several tests have been used to find out if a person has been exposed to toluene. These include measuring toluene and its breakdown products in blood and in urine. These tests are not commonly available at a doctor's office, but are easily done by special laboratories. To decide whether workplace exposure to toluene has happened, measurements of one of its breakdown products in urine have been used within 12 hours after exposure. However, because several other chemicals are also changed to the same breakdown product within the body, this test may not show that toluene exposure has happened. Other things, such as the amount of body fat and body weight, the person's sex, and exposure conditions, may also change this estimate of the amount of toluene exposure.

What levels of exposure have resulted in harmful health effects?

Toluene can be smelled in air at a level of about 0.16 ppm and it can be smelled in water at a level of 0.04 ppm. In water, toluene can be tasted at a level of 0.04 ppm. Tables 1-1, 1-2, 1-3, and 1-4 show the relationship between exposure to toluene and known health effects. Minimal Risk Levels (MRLs) are also included in Table 1-1. These MRLs were derived based on animal data for both short-term and longer-term exposure. The MRLs provide a basis for comparison to levels of toluene which people might encounter either in the air or in food or drinking water. If a person is exposed to toluene at an amount below the MRL, it is not expected that harmful noncancer health effects will occur. Since these levels are based on information that is currently available, there is always some uncertainty associated with it. Also, since the method for deriving MRLs does not use any information about cancer, an MRL does not imply anything about the presence, absence, or level of risk of cancer.

What recommendations has the federal government made to protect human health?

The federal government has developed regulatory standards and advisories to protect people from the possible health effects of toluene in the environment. The Occupational Safety and Health Administration (OSHA) has set a limit of 100 ppm of toluene for air in the workplace, averaged for an 8-hour exposure per day over a 40-hour workweek. The American Conference of Governmental Industrial Hygienists (ACGIH) and the National Institute for Occupational Safety and Health (NIOSH) have recommended that toluene in the workplace not exceed 100 ppm (as an average level over 8 hours).

EPA has recommended that drinking water should not contain more than 20 ppm for 1 day or 3 ppm for 10 days or 1 ppm for lifetime consumption. Any release of more than 1000 lbs of this chemical to the environment must be reported to the National Response Center. More information on state guidelines for air and water are available from state environmental agencies.

Where can I get more information?

If you have more questions or concerns, please contact your state health or environmental department or:

Agency for Toxic Substances and Disease Registry
Division of Toxicology
1600 Clifton Road, E-29
Atlanta, Georgia 30333

ATSDR **ToxFAQs**

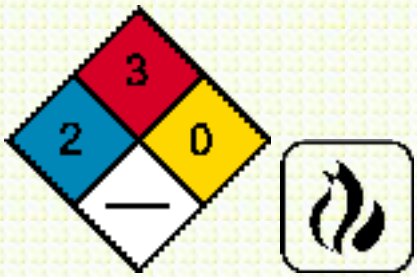
Toluene

CAS# 108-88-3

September 1995

Toluene
C_7H_8
Stereo Image
XYZ File

Search ChemFinder



NFPA Label Key

Material Safety Data Sheet
(University of Utah)

Agency for Toxic Substances and Disease Registry

This fact sheet answers the most frequently asked health questions about toluene. For more information, you may call the ATSDR Information Center at 1-800-447-1544. This fact sheet is one in a series of summaries about hazardous substances and their health effects. This information is important because this substance may harm you. The effects of exposure to any hazardous substance depend on the dose, the duration, how you are exposed, personal traits and habits, and whether other chemicals are present.

SUMMARY: Exposure to toluene happens mostly through breathing it in workplace air, in automobile exhaust, or during deliberate glue sniffing or solvent abuse. It is also used in many consumer products. Breathing high levels of toluene affects the brain and can cause headaches, confusion, dizziness, sleepiness, and memory loss. This chemical has been found in at least 869 of 1,416 National Priorities List sites identified by the Environmental Protection Agency.

What is toluene?
(Pronounced tol'yoo-een')

Toluene is a colorless liquid with a distinctive sweet and pungent smell. It occurs naturally in crude oil and in the tolu tree. You can smell toluene at 8 parts of toluene per million parts of air (ppm) and taste it in water at 0.04 ppm to 1 ppm.

Toluene is produced during the process of making gasoline and other fuels from crude oil, in making coke from coal, and as a by-product in the manufacture of styrene.

It is also used in making paints, paint thinners, fingernail polish, lacquers, adhesives, and rubber and in some printing and leather tanning processes.

What happens to toluene when it enters the environment?

- Toluene has been found in waste sites and landfills when discarded as used solvent or in paints, paint thinners, and nail polish.
- It does not stay in the environment long.
- It is readily broken down by microorganisms in the soil.
- It evaporates quickly from the soil and surface water into the air.
- Toluene in the air combines with oxygen to form benzaldehyde and cresol, which can be harmful to people.
- Toluene can be taken up by fish, shellfish, plants, and animals living in water, but high levels do not build up.

How might I be exposed to toluene?

- People may be exposed through breathing toluene in workplace air or in automobile exhaust.
- Sniffing glue or using solvents improperly could lead to high exposures.
- Breathing contaminated air or touching it when working with gasoline, kerosene, heating oil, paints, and lacquers puts people at the greatest risk of exposure to toluene in air and on the skin.
- High exposures can occur at home and outdoors while using gasoline, nail polish, rubber cement, paints, paintbrush cleaners, stain removers, fabric dyes, inks, and adhesives.
- Drinking contaminated water or breathing air near waste sites and landfills could lead to higher exposures.
- The amount of toluene in food is likely to be low.
- People are also exposed to toluene by breathing cigarette smoke that has small amounts of toluene in it.

How can toluene affect my health?

Toluene affects the brain. Low-to-moderate levels from long-term exposure can cause tiredness, confusion, weakness, drunken-type actions, memory loss, nausea and loss of appetite, and hearing loss.

Inhaling a high level of toluene in a short time can make you feel light-headed, dizzy, or sleepy. It can cause unconsciousness, and even death.

Repeated exposure to high levels can cause permanent brain and speech damage, vision and hearing problems, loss of muscle control, and poor balance. It can also cause memory loss and decreased mental ability.

Toluene also affects the kidneys.

Several studies have shown that unborn animals were harmed when high levels of toluene were breathed by their mothers. Babies can have neurologic problems and retarded growth and development if their mothers breathe a high level of toluene during pregnancy. We do not know if toluene harms the unborn child if the mother is exposed to low levels of toluene during pregnancy.

How likely is toluene to cause cancer?

The Department of Health and Human Services and the International Agency for Research on Cancer have not classified toluene for carcinogenic effects. Studies in workers and animals indicate that toluene does not cause cancer.

Is there a medical test to show whether I've been exposed to toluene?

Laboratory tests can detect toluene or its breakdown products in exhaled air, blood, or urine. These tests are only useful within 12 hours of exposure and do not tell if harmful effects will occur. These tests are not routinely available at your doctor's office.

Has the federal government made recommendations to protect human health?

The Environmental Protection Agency (EPA) has set a limit in drinking water of 1 ppm toluene. EPA recommends that children should not drink water containing more than 20 ppm toluene for 1 day, or 2 ppm for longer lengths of time (7 years). Adults should not drink water containing more than 7 ppm toluene for longer times.

The EPA requires that spills or accidental releases of toluene into the environment of 1,000 pounds or more must be reported to EPA.

The Occupational Safety and Health Administration (OSHA) set a maximum level of 200 ppm toluene in workplace air for an 8-hour workday, 40-hour workweek.

The National Institute for Occupational Safety and Health (NIOSH) recommends an exposure limit of 100 ppm of toluene in workplace air and the American Conference of Governmental Industrial Hygienists (ACGIH) recommends an exposure limit of 50 ppm in workplace air.

Glossary

Carcinogenic:

Ability to cause cancer.

Long-term:

Lasting one year or longer.

PPM:

Parts per million.

References

Agency for Toxic Substances and Disease Registry (ATSDR). 1994. Toxicological profile for toluene (update). Atlanta, GA.: U.S. Department of Health and Human Services, Public Health Service.

Where can I get more information?

ATSDR can tell you where to find occupational and environmental health clinics. Their specialists can recognize, evaluate, and treat illnesses resulting from exposure to hazardous substances. You can also contact your community or state health or environmental quality department if you have any more questions or concerns.

For more information, contact:

Agency for Toxic Substances and Disease Registry
Division of Toxicology
1600 Clifton Road NE, Mailstop E-29
Atlanta, GA 30333
Phone: 1-800-447-1544
FAX: 404-639-6315



U.S. Department of Health and Human Services
Public Health Service
Agency for Toxic Substances and Disease Registry

Link to ToxFAQs Home Page

Link to ATSDR Science Corner

Link to ATSDR Home Page

TOLUENE

Toluene is a federal hazardous air pollutant and was identified as a toxic air contaminant in April 1993 under AB 2728.

CAS Registry Number: 108-88-3

Molecular Formula: C_7H_8

Description

Toluene is a colorless, flammable, non-corrosive liquid with a benzene-like odor. It is insoluble in water and soluble in acetone, absolute alcohol, ether, chloroform, benzene, petroleum ether, glacial acetic acid, and carbon disulfide (HSDB, 1991).

Physical Properties of Toluene

Molecular Weight	92.13
Boiling Point	110.7 oC
Melting Point	-95 oC
Flash Point	40 oF (closed cup)
Vapor Density	3.2 (air = 1)
Vapor Pressure	36.7 mm Hg at 30 oC
Density/Specific Gravity	0.866 at 20/4 oC (water = 1)
Log Octanol/Water Partition Coefficient	2.69
Conversion Factor	1 ppm = 3.77 mg/m3

(HSDB, 1991; Merck, 1989; Sax, 1987; Sax, 1989; U.S. EPA, 1994a)

SOURCES AND EMISSIONS

A. Sources

Toluene is used in aviation gasoline and high-octane blending stock, and as a solvent for paints, coatings, gums and resins. Other sources include tobacco smoke, petroleum and coal production, use as a chemical intermediate, and for styrene production.

The primary stationary sources that have reported emissions of toluene in California are crude petroleum and natural gas extraction, petroleum refining, and household furniture manufacturing facilities (ARB, 1997b). Toluene has also been detected but not quantified in motor vehicle exhaust by the Air Resources Board (ARB) (ARB, 1995e).

Toluene was registered for use as a pesticide; however, as of January 1, 1987, it is no longer registered for pesticidal use in California (DPR, 1996).

B. Emissions

The total emissions of toluene from stationary sources in California are estimated to be at least 5.4 million pounds per year, based on data reported under the Air Toxics "Hot Spots" Program (AB 2588) (ARB, 1997b). In addition, ARB staff estimates that 12.6 million and 62 thousand pounds per year are emitted from area and natural sources, respectively (ARB, 1990b).

C. Natural Occurrence

Natural sources of toluene include volcanos, forest fires, and crude oil (HSDB, 1991).

AMBIENT CONCENTRATIONS

Toluene is routinely monitored by the statewide ARB air toxics network. The network's mean concentration of toluene from January 1996 through December 1996 is estimated to be 8.29 micrograms per cubic meter (µg/m3) or 2.2 parts per billion (ppb) (ARB 1997c).

The United States Environmental Protection Agency (U.S. EPA) has also reported concentrations of toluene from 14 study areas during 1989 to 1991. The overall mean concentration from these areas was 10.2 µg/m3 (2.7 ppb) (U.S. EPA 1993a).

INDOOR SOURCES AND CONCENTRATIONS

Environmental tobacco smoke (ETS) emissions of toluene were measured using six cigarette brands popular in California and one reference cigarette. Toluene had an average emission of 656 µg/cigarette (Daisey et al., 1994).

There have been studies that have measured toluene within vehicles. A southern California study measured an average toluene in-vehicle concentration of 136.5 µg/m3 (36.3 ppb) and a maximum concentration of 994.6 µg/m3 (264.5 ppb) during the summer of 1987 and winter of 1988 (Shikiya et al., 1989). Similar studies in Raleigh, North Carolina and Boston, Massachusetts measured average concentrations of 33.3 and 46.5 µg/m3 (8.9 and 12.4 ppb) and maximum concentrations of 105 and 118.9 µg/m3 (27.9 and 31.6 ppb), respectively (Chan et al., 1991a; Chan et al., 1991b). These studies found toluene concentrations to be 2 to 5 times greater than outdoor toluene concentrations.

ATMOSPHERIC PERSISTENCE

Toluene exists in the atmosphere in the gas phase, and the dominant tropospheric loss process is by reaction with the OH radical. The calculated half-life and lifetime of toluene due to reaction with the OH radical are 1.7 days and 2.4 days, respectively (Atkinson, 1995). The reaction products include benzaldehyde, benzyl nitrate, cresols, glyoxal, methylglyoxal, and poorly understood ring-opened

compounds (Atkinson, 1994).

AB 2588 RISK ASSESSMENT INFORMATION

The Office of Environmental Health Hazard Assessment reviews risk assessments submitted under the Air Toxics "Hot Spots" Program (AB 2588). Of the risk assessments reviewed as of December 1996, for non-cancer health effects, toluene contributed to the total hazard index in 51 of the approximately 89 risk assessments reporting a total chronic hazard index greater than 1. Toluene also contributed to a total hazard index greater than 1 in 7 of the approximately 107 risk assessments reporting a total acute hazard index greater than 1, and presented an individual hazard index greater than 1 in 1 of these risk assessments (OEHHA, 1996b).

HEALTH EFFECTS

The most probable route of human exposure to toluene is inhalation (HSDB, 1991).

Non-Cancer: Exposure to toluene may cause mild eye and respiratory tract irritation. The central nervous system (CNS) is the primary target organ for acute and chronic exposures. Toluene is a CNS depressant. Exposure may cause cardiac arrhythmias. Liver and kidney injury may occur with exposures to high concentrations. Long-term abuse by inhalation has caused CNS impairment (U.S. EPA, 1994a).

A chronic non-cancer Reference Exposure Level (REL) of 200 µg/m3 is listed for toluene in the California Air Pollution Control Officers Association Air Toxics "Hot Spots" Program, Revised 1992 Risk Assessment Guidelines. The toxicological endpoints considered for chronic toxicity are the central or peripheral nervous system, and the reproductive system including teratogenic and developmental effects (CAPCOA, 1993). The U.S. EPA has established a Reference Concentration (RfC) of 400 µg/m3 for toluene based on neurological effects in humans. The U.S. EPA estimates that inhalation of this concentration or less, over a lifetime, would not likely result in the occurrence of chronic non-cancer effects. The U.S. EPA has established an oral Reference Dose of 0.2 milligrams per kilogram per day based on changes in liver and kidney weights in rats. The U.S. EPA estimates that consumption of this dose or less, over a lifetime, would not likely result in the occurrence of chronic, non-cancer effects.

Children of pregnant women exposed to toluene by inhalation have been reported to have developmental effects, such as CNS dysfunction, attention deficits, and minor craniofacial and limb anomalies; however, these studies were confounded by exposure to multiple chemicals. A number of case reports of toluene abuse via inhalation by pregnant women have also shown similar effects. Reproductive effects, including an association between paternal exposure to toluene and an increased odds ratio for spontaneous abortions but not birth defects, have also been noted. However, these studies are not conclusive due to many confounding variables. Several inhalation studies have shown toluene to be a developmental toxicant, but not a reproductive toxicant, in rodents (U.S. EPA, 1994a). The State of California under Proposition 65 has determined that toluene is a developmental toxicant (CCR, 1996).

Cancer: Two epidemiological studies did not detect a statistically significant increased risk of cancer due to inhalation exposure to toluene. However, these studies were limited due to the size of the study population and lack of historical monitoring data. The U.S. EPA has placed toluene in Group D: Not classifiable as a carcinogen (U.S. EPA, 1994a). The International Agency for Research on Cancer has

placed toluene in Group 3: Not classifiable as a carcinogen (IARC, 1989b).

EPA United States Environmental Protection Agency
Office of Air Quality Planning & Standards OAQPS
TTNWeb Technology Transfer Network
UATW Unified Air Toxics Website

TOLUENE

108-88-3

Hazard Summary

CAUTION: Unless otherwise noted, the quantitative information on these fact sheets are from "EPA Health Effects Notebook for Hazardous Air Pollutants-Draft", EPA-452/D-95-00, PB95-503579, December 1994." Please conduct a current literature search and check the appropriate current online database for the most recent quantitative information.

- The central nervous system (CNS) is the primary target organ for toluene toxicity in both humans and animals for acute (short-term) and chronic (long-term) exposures. **CNS dysfunction** (which is often reversible) and **narcosis** have been frequently observed in humans acutely exposed to low or moderate levels of toluene by inhalation; symptoms include fatigue, sleepiness, headaches, and nausea. Cardiac arrhythmia has also been reported in humans acutely exposed to toluene.
- **CNS depression** has been reported to occur in chronic abusers exposed to high levels of toluene. Symptoms include ataxia, tremors, cerebral atrophy, nystagmus (involuntary eye movements), and impaired speech, hearing, and vision. Chronic inhalation exposure of humans to toluene also causes irritation of the upper respiratory tract, eye irritation, sore throats, nausea, skin conditions, dizziness, headaches, and difficulty with sleep.
- The Reference Concentration (RfC) for toluene is 0.4 mg/m^3.[a] The U.S. Environmental Protection Agency (EPA) estimates that inhalation of this concentration or less, over a lifetime, would not likely result in the occurrence of chronic, noncancer effects.[b]
- The Reference Dose (RfD) for toluene is 0.2 mg/kg/d.[c] EPA estimates that consumption of this dose or less, over a lifetime, would not result in the occurrence of chronic, noncancer effects.
- Human studies have reported developmental effects, such as CNS dysfunction, attention deficits, and minor craniofacial and limb anomalies, in the children of pregnant women exposed to toluene or mixed solvents by inhalation. Reproductive effects, including an association between paternal exposure to toluene and an increased odds ratio for spontaneous abortions but not birth defects, have also been noted. However, these studies are not conclusive due to many confounding variables. Animal studies have shown toluene to have developmental, but not reproductive, effects from inhalation exposure.
- None of the data suggest that toluene is carcinogenic. Two epidemiological studies did not detect a statistically significant increased risk of cancer due to inhalation exposure to toluene. However,

these studies had many confounding factors. Animal studies have been negative for carcinogenicity. EPA has classified toluene as a Group D, **not classifiable as to human carcinogenicity**.

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[a] Milligrams per cubic meter is the unit of measurement for chemicals in air.

[b] The RfC is not a direct estimator of risk but rather a reference point to gauge the potential effects. Exceedance of the RfC does not imply that an adverse health effect would necessarily occur. As the amount and frequency of exposures exceeding the RfC increase, the probability of adverse health effects also increases.

[c] Milligrams per kilogram per day is one way to measure the amount of the contaminant that is consumed in food.

Please Note: The main sources of information for this fact sheet are EPA's Integrated Risk Information System (IRIS), which contains information on inhalation chronic toxicity of toluene and the RfC, oral chronic toxicity and the RfD, and the carcinogenic effects of toluene, and the Agency for Toxic Substances and Disease Registry's (ATSDR's) *Toxicological Profile for Toluene*. Other secondary sources include the Hazardous Substances Data Bank (HSDS), a database of summaries of peer-reviewed literature, and the Registry of Toxic Effects of Chemical Substances (RTECS), a database of toxic effects that are not peer reviewed.

Environmental/Occupational Exposure

- The highest concentrations of toluene usually occur in indoor air from the use of common household products (paints, paint thinners, and adhesives) and cigarette smoke. The deliberate inhalation of paint or glue may produce high levels of exposure to toluene, as well as to other chemicals, in solvent abusers. (1)
- Toluene exposure may also occur in the workplace, especially in occupations such as printing or painting, where toluene is frequently used as a solvent. (1)
- Automobile emissions are the principal source of toluene to the ambient air. Toluene may also be released to the ambient air during the production, use, and disposal of industrial and consumer products that contain toluene. (1)

Assessing Personal Exposure

- Toluene and its breakdown products can be detected in the blood or urine to determine whether or not exposure has occurred. Metabolites measured in the urine are not specific to toluene, and testing must occur within 12 hours of exposure. (1)

Health Hazard Information

Acute Effects:

- The central nervous system is the primary target organ for toluene toxicity in both humans and animals for acute (short-term) and chronic (long-term) exposures. CNS dysfunction (which is often reversible) and narcosis have been frequently observed in humans acutely exposed to low or moderate levels of toluene by inhalation; symptoms include fatigue, sleepiness, headaches, and

nausea. CNS depression and death have occurred at higher levels of exposure. (1)

- Cardiac arrhythmia has also been reported in humans acutely exposed to toluene. (1)
- Following the ingestion of toluene a person died from a severe depression of the central nervous system. Constriction and necrosis of myocardial fibers, swollen liver, congestion and hemorrhage of the lungs, and tubular kidney necrosis were also reported. (1)
- Acute exposure of animals to toluene has been reported to affect the central nervous system as well as to decrease resistance to respiratory infection. (1)
- Acute animal tests, such as the LC_{50} and LD_{50} tests in rats and mice, have demonstrated toluene to have low acute toxicity by inhalation or oral exposure. (1)

Chronic Effects (Noncancer):

- CNS depression has been reported to occur in chronic (long-term) abusers exposed to high levels of toluene. Symptoms include ataxia, tremors, cerebral atrophy, nystagmus (involuntary eye movements), and impaired speech, hearing, and vision. (1,2)
- Effects on the central nervous system have also been observed in studies of animals chronically exposed by inhalation. (1,2)
- Chronic inhalation exposure of humans to toluene causes irritation of the upper respiratory tract, eye irritation, sore throats, nausea, skin conditions, dizziness, headaches, and difficulty with sleep. (1,2)
- Inflammation and degeneration of the nasal and respiratory epithelium and pulmonary lesions have been observed in rats and mice chronically exposed to high levels of toluene by inhalation. (1)
- Mild effects on the kidneys and liver have been reported in solvent abusers chronically exposed to toluene vapor. However, these studies are confounded by probable exposure to multiple solvents. (1,2)
- Slight adverse effects on the liver, kidneys, and lung have been reported in some chronic inhalation studies of rodents. (1)
- The RfC for toluene is 0.4 mg/m^3 based on neurological effects in humans. (2)
- EPA has medium confidence in the study on which the RfC was based because it indicates adverse neurological effects of toluene in a small worker population; medium confidence in the database because even though many chronic laboratory animal studies are available, long-term data in humans are not available for either the neurotoxicity or irritation endpoint; and, consequently, medium confidence in the RfC. (2)
- The RfD for toluene is 0.2 mg/kg/d based on changes in liver and kidney weights in rats. (2)
- EPA has high confidence in the study on which the RfD was based because a sufficient number of animals/sex were tested in each of six dose groups and many parameters were studied; medium confidence in the database because it is supported by a 6-month oral study; and, consequently, medium confidence in the RfD. (2)
- EPA's Office of Air Quality Planning and Standards, for a hazard ranking under Section 112(g) of the Clean Air Act Amendments, has evaluated toluene for chronic toxicity and has given it a composite score of 7 (scores range from 1 to 100, with 100 being the most toxic). These scores are nonlinear and are the product of two ratings: a rating based on the minimal-effect-dose and a rating based on the type of effect. (3)

Reproductive/Developmental Effects:

- CNS dysfunction, attention deficits, minor craniofacial and limb anomalies, and developmental delay were observed in the children of pregnant women exposed to toluene or to mixed solvents by inhalation. Growth retardation and dysmorphism were reported in infants of another study. However, these studies were confounded by exposure to multiple chemicals. (1,2)
- Children born to toluene abusers have exhibited temporary renal tubular acidosis. (1)
- Paternal exposure (in which the mothers had no occupational exposure to toluene but the fathers did) increased the odds ratio for spontaneous abortions but not congenital malformations. However, these observations cannot be clearly ascribed to toluene because of the small number of cases evaluated and the large number of confounding variables. (1)
- Several inhalation studies have shown toluene to be a developmental toxicant, but not a reproductive toxicant, in rodents. (1)

Cancer Risk:

- Two epidemiological studies did not detect a statistically significant increased risk of cancer due to inhalation exposure to toluene. However, these studies were limited due to the size of the study population and lack of historical monitoring data. (1)
- Inhalation exposure of rats did not produce an increased incidence of treatment-related neoplastic lesions. (1,2)
- EPA has classified toluene as a Group D, not classifiable as to human carcinogenicity. (2)

Physical Properties

- The chemical formula for toluene is $C_6H_5CH_3$, and its molecular weight is 92.15 g/mol. (1,4)
- Toluene occurs as a colorless, flammable, refractive liquid, that is slightly soluble in water. (1,5)
- Toluene has a sweet, pungent odor, with an odor threshold of 2.9 ppm. (1,6)
- The vapor pressure for toluene is 22 mm Hg at 20 C, and its log octanol/water partition coefficient (log K_{ow}) is 2.79. (1)

Uses

- The major use of toluene is as a mixture added to gasoline to improve octane ratings. Toluene is also used to produce benzene and as a solvent in paints, coatings, adhesives, inks, and cleaning agents. (1)
- Toluene is also used in the production of polymers used to make nylon, plastic soda bottles, and polyurethanes and for pharmaceuticals, dyes, cosmetic nail products, and the synthesis of organic chemicals. (1)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) × (molecular weight of the compound)/(24.45). For toluene: 1 ppm = 3.77 mg/m^3.

Health Data from Inhalation Exposure

Concentration (mg/m^3)	Health numbers[a]	Regulatory, advisory numbers[b]	Reference
100,000.0			
-- -- -- -- 10,000.0	• LC_{50} (rats) ($33,176\ mg/m^3$) • LC_{50} (mice) ($20,056\ mg/m^3$)		1 1
-- -- -- -- 1,000.0			
-- -- -- -- 100.0	• LOAEL (humans) ($332\ mg/m^3$)	• ACGIH TLV, NIOSH REL, OSHA PEL, MSHA ($75\ mg/m^3$)	2 7
-- -- -- -- 10.0			
-- -- -- -- 1.0			
-- -- -- -- 0.1	• RfC ($0.4\ mg/m^3$)		2

ACGIH TLV--American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.
LC_{50} (Lethal $Concentration_{50}$)--A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.
LOAEL--Lowest-observed-adverse-effect level.
MSHA--Mine Safety and Health Administration.

NIOSH REL--National Institute of Occupational Safety and Health's recommended exposure limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling.
OSHA PEL--Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.
RfC--Reference concentration.

[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.

References

1. Agency for Toxic Substances and Disease Registry (ATSDR). *Toxicological Profile for Toluene* (Draft). U.S. Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA. 1992.
2. U.S. Environmental Protection Agency. *Integrated Risk Information System (IRIS) on Toluene*. Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development, Cincinnati, OH. 1993.
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7. U.S. Department of Health and Human Services. Registry of Toxic Effects of Chemical Substances (RTECS, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

Toluene

CASRN 108-88-3

Contents

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VIII. SYNONYMS

0118
Toluene; CASRN 108-88-3

Health assessment information on a chemical substance is included in IRIS only after a comprehensive review of chronic toxicity data by U.S. EPA health scientists from several Program Offices and the Office of Research and Development. The summaries presented in Sections I and II represent a consensus reached in the review process. Background information and explanations of the methods used to derive the values given in IRIS are provided in the Background Documents.

STATUS OF DATA FOR Toluene

File On-Line 01/31/1987

Category (section)	Status	Last Revised
Oral RfD Assessment (I.A.)	on-line	04/01/1994
Inhalation RfC Assessment (I.B.)	on-line	08/01/1992

Carcinogenicity Assessment (II.) on-line 02/01/1994

_I. CHRONIC HEALTH HAZARD ASSESSMENTS FOR NONCARCINOGENIC EFFECTS

__I.A. REFERENCE DOSE FOR CHRONIC ORAL EXPOSURE (RfD)

Substance Name -- Toluene
CASRN -- 108-88-3
Last Revised -- 04/01/1994

The oral Reference Dose (RfD) is based on the assumption that thresholds exist for certain toxic effects such as cellular necrosis. It is expressed in units of mg/kg-day. In general, the RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. Please refer to the Background Document for an elaboration of these concepts. RfDs can also be derived for the noncarcinogenic health effects of substances that are also carcinogens. Therefore, it is essential to refer to other sources of information concerning the carcinogenicity of this substance. If the U.S. EPA has evaluated this substance for potential human carcinogenicity, a summary of that evaluation will be contained in Section II of this file.

___I.A.1. ORAL RfD SUMMARY

Critical Effect	Experimental Doses*	UF	MF	RfD
Changes in liver and kidney weights 13-Week Rat Gavage Study NTP, 1989	NOAEL: 312 mg/kg converted to 223 mg/kg/day LOAEL: 625 mg/kg converted to 446 mg/kg/day	1000	1	2E-1 mg/kg/day

*Conversion Factors: Dose adjusted for gavage schedule of 5 days/week.

I.A.2. PRINCIPAL AND SUPPORTING STUDIES (ORAL RfD)

NTP (National Toxicology Program). 1989. Toxicology and Carcinogenesis Studies of toluene in F344/N rats and B6C3F1 mice. Technical Report Series No. 371. Research Triangle Park, NC.

The oral toxicity of toluene was investigated in this subchronic gavage study in F344 rats. Groups of 10 rats/sex/group were administered toluene in corn oil at dosage levels of 0, 312, 625, 1250, 2500, or 5000 mg/kg for 5 days/week for 13 weeks. All animals receiving 5000 mg/kg died within the first week. One female and 8 males in the 2500 mg/kg group died, but 2 of these were due to gavage errors. No deaths occurred at lower doses. Several toxic effects were noted at doses greater than or equal to 2500 mg/kg, including prostration, hypoactivity, ataxia, piloerection, lacrimation, excessive salivation, and body tremors. No signs of biologic significance were seen in groups receiving less than or equal to 1250 mg/kg. The only significant change in body weight was a decrease ($p<0.05$) for males in the 2500 mg/kg group. There were no toxicologically significant changes in hematology or urinalysis for any group of animals. Biochemical changes, including a significant increase ($p<0.05$) in SGOT in 2500 males and a dose-related increase in cholinesterase in females receiving 2500 and 5000 mg/kg, were not considered to be biologically significant. There were several pathologic findings and organ weight changes in the liver, kidney, brain, and urinary bladder. In males, absolute and relative weights of both the liver and kidney were significantly increased ($p<0.05$) at doses greater than or equal to 625 mg/kg. In females, absolute and relative weights of the liver, kidney, and heart were all significantly increased at doses greater than or equal to 1250 mg/kg ($p<0.01$ for all comparisons except $p<0.05$ for absolute kidney and heart weights at 1250 mg/kg). Histopathologic lesions in the liver consisted of hepatocellular hypertrophy, occurring at greater than or equal to 2500 mg/kg. Nephrosis was observed in rats that died, and damage to the tubular epithelia of the kidney occurred in terminally sacrificed rats. Histopathologic changes were also noted in the brain and urinary bladder. In the brain, mineralized foci and necrosis of neuronal cells were observed in males and females at 2500 mg/kg and males at 1250 mg/kg. In the bladder, hemorrhage of the muscularis was seen in males and females at 5000 mg/kg and males at 2500 mg/kg. The NOAEL for this study is 312 mg/kg/day based on liver and kidney weight changes in male rats at 625 mg/kg. The toxicologic significance of these organ weight changes is strengthened by the occurrence of histopathologic changes in both the liver and kidney at higher doses. Because the exposure was for 5 days/week, this dose is converted to 312 x 5/7 = 223 mg/kg/day. The LOAEL is 625 mg/kg, which is 446 mg/kg/day when converted.

NTP (1989) also conducted a 13-week gavage study in B6C3F1 mice, following the same regimen described above. All mice receiving 5000 mg/kg died and 8/20 receiving 2500 mg/kg also died. Signs of toxicity seen in animals receiving greater than or equal to 2500 mg/kg included subconvulsive jerking, prostration, impaired grasping reflex, bradypnea, hypothermia, ataxia, and hypoactivity. By week 13, the mean body weight of 2500 mg/kg males was significantly ($p<0.05$) lower than controls. No other significant changes were reported for any group, including macroscopic observation, organ weight means,

or clinical pathology parameters. The NOAEL for mice in this study was 1250 mg/kg.

The subchronic study by Wolf et al. (1956) is supportive of the NTP studies. Groups of 10 female Wistar rats were administered gavage doses of 0, 118, 354, or 590 mg/kg toluene dissolved in olive oil. A total of 138 doses were administered over 193 days, resulting in average doses of approximately 0, 84, 253, or 422 mg/kg/day. Hematologic, behavioral, gross and histopathologic examinations were conducted with no toxic effects being reported at any dose. Therefore, the highest dose of 422 mg/kg/day is considered to be the NOAEL for this study. However, this study is not used as the basis for the RfD because the LOAEL of 446 mg/kg/day identified by NTP (1989) is too close to the NOAEL identified by Wolf et al. (1956). Also, the NTP study indicated that male rats are more sensitive to toluene and the Wolf study utilized only female rats.

___I.A.3. UNCERTAINTY AND MODIFYING FACTORS (ORAL RfD)

UF -- An uncertainty factor of 1000 was applied to account for inter- and intraspecies extrapolations, for subchronic-to-chronic extrapolation and for limited reproductive and developmental toxicity data.

MF -- None

___I.A.4. ADDITIONAL COMMENTS (ORAL RfD)

Kostas and Hotchin (1981) exposed NYLAR mice pre- and post-natally to toluene provided in the drinking water at concentrations of 0, 16, 80, or 400 ppm. Effects were noted in all dosed groups on rotorod performance, measured at 45 to 55 days of age, but there was an inverse dose-response relationship. No effects of toluene exposure were seen on maternal fluid consumption, offspring mortality rate, development of eye or ear openings, or surface-righting response. This study is not suitable for use in risk assessment because only 6 to 9 pregnancies/dose group were obtained, and because the dose-response relationship was inverse.

In an abstract providing limited information, Nawrot and Staples (1979) reported an increase in embryonic lethality in mice exposed to toluene from days 6 to 15 of gestation. Pregnant CD-1 dams were administered 0.3, 0.5, or 1.0 mL/kg bw, 3 times/day (equivalent to approximately 780, 1300, or 2600 mg/kg/day). Maternal toxicity was not observed at any dose level, but toluene was shown to be teratogenic at the high dose and embryolethal at the low dose. These levels are higher than the NOAEL demonstrated by the NTP (1989) study.

Several subchronic and chronic inhalation studies have been performed on toluene but are not considered to be suitable for deriving an oral RfD. These

studies are summarized nicely in the introduction to the 2-year inhalation bioassay by NTP, 1989. The studies identify the following potential target organs: kidney (male rat); hematologic effects (mice); central nervous system (rats, mice, primates); developmental toxicity (rats, rabbits). It is beyond the scope of this oral RfD summary sheet to describe each of these studies, but the two chronic (2 year) inhalation studies are summarized briefly below.

In a 2-year inhalation study by NTP (1989), F344 rats (60/sex/group) were exposed to 0, 600, or 1200 ppm toluene and B6C3F1 mice (60/sex/group) to 0, 120, 600, or 1200 ppm toluene for 6.5 hours/day, 5 days/week. Ten animals/group (except male mice) were removed at 15 months for toxicologic evaluation. At 15 months, there was an increased incidence and severity of nonneoplastic lesions of the nasal cavity of exposed rats. Minimal hyperplasia of the bronchial epithelium was seen in 4/10 female mice at 1200 ppm. There were no significant differences in survival among any group of animals during the 2-year study. Mean body weights were generally similar for all groups throughout the study. Nephropathy was seen in almost all rats with the severity somewhat increased in exposed rats. There were also effects on the olfactory and respiratory epithelia of exposed rats. No biologically important lesions were seen in any groups of mice. There was no evidence of carcinogenicity for any group of animals in this study.

A chronic inhalation study in rats performed by CIIT (1980) failed to produce an adverse effect. Groups of 40 F344 rats/sex were exposed to 30, 100, or 300 ppm toluene for 6 hours/day, 5 days/week for 24 months. An unexposed group of 120 rats/sex served as a control. Clinical chemistry, hematology, and urinalysis testing were conducted at 18 and 24 months. All parameters measured at the termination of the study were normal except for a dose-related reduction in hematocrit values in females exposed to 100 and 300 ppm toluene. The highest dose of 300 ppm was considered to be a NOAEL.

___I.A.5. CONFIDENCE IN THE ORAL RfD

Study: High
Data Base: Medium
RfD: Medium

Confidence in the principal study is high because a sufficient number of animals/sex were tested in each of six dose groups (including vehicle controls) and many parameters were studied. The same protocol was tested in both mice and rats, with rats being identified as the more sensitive species. The data base is rated medium because it is supported by a 6-month oral study. It is not higher than medium because there is no reproductive study. Also, the oral studies are all subchronic, with the critical study being only 13 weeks in duration. Medium confidence in the RfD follows.

___I.A.6. EPA DOCUMENTATION AND REVIEW OF THE ORAL RfD

Source Document -- This assessment is not presented in any existing U.S. EPA document.

Other EPA Documentation -- None

Agency Work Group Review -- 05/20/1985, 08/05/1985, 08/05/1986, 05/17/1990, 06/20/1990

Verification Date -- 06/20/1990

___I.A.7. EPA CONTACTS (ORAL RfD)

Please contact the Risk Information Hotline for all questions concerning this assessment or IRIS, in general, at (513)569-7254 (phone), (513)569-7159 (FAX) or RIH.IRIS@EPAMAIL.EPA.GOV (internet address).

__I.B. REFERENCE CONCENTRATION FOR CHRONIC INHALATION EXPOSURE (RfC)

Substance Name -- Toluene
CASRN -- 108-88-3
Last Revised -- 08/01/1992

The inhalation Reference Concentration (RfC) is analogous to the oral RfD and is likewise based on the assumption that thresholds exist for certain toxic effects such as cellular necrosis. The inhalation RfC considers toxic effects for both the respiratory system (portal-of-entry) and for effects peripheral to the respiratory system (extrarespiratory effects). It is expressed in units of mg/cu.m. In general, the RfC is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily inhalation exposure of the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. Inhalation RfCs were derived according to the Interim Methods for Development of Inhalation Reference Doses (EPA/600/8-88/066F August 1989) and subsequently, according to Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry (EPA/600/8-90/066F October 1994). RfCs can also be derived for the noncarcinogenic health effects of substances that are carcinogens. Therefore, it is essential to refer to other sources of information concerning the carcinogenicity of this substance. If the U.S. EPA

has evaluated this substance for potential human carcinogenicity, a summary of that evaluation will be contained in Section II of this file.

___I.B.1. INHALATION RfC SUMMARY

Critical Effect	Exposures*	UF	MF	RfC
Neurological effects	NOAEL: None	300	1	4E-1 mg/cu.m
Occupational Study Foo et al., 1990	LOAEL: 332 mg/cu.m (88 ppm) LOAEL(ADJ): 119 mg/cu.m LOAEL(HEC): 119 mg/cu.m			
Degeneration of nasal epithelium 2-Year Rat Chronic Inhalation Study NTP, 1990	NOAEL: None LOAEL: 2261 mg/cu.m (600 ppm) LOAEL(ADJ): 437 mg/cu.m LOAEL(HEC): 79 mg/cu.m			

*Conversion Factors: MW = 92.15.

Foo et al., 1990: Assuming 25 C and 760 mmHg, LOAEL (mg/cu.m) = 88 ppm x 92.15/24.45 = 332 mg/cu.m. This is an extrarespiratory effect of a soluble vapor. The LOAEL is based on an 8-hour TWA occupational exposure. MVho = 10 cu.m/day, MVh = 20 cu.m/day. LOAEL(HEC) = LOAEL(ADJ) = 332 x MVho/MVh x 5 days/7 days = 119 mg/cu.m.

NTP, 1990: Assuming 25 C and 760 mmHg, LOAEL (mg/cu.m) = 600 ppm x 92.15/24.45 = 2261 mg/cu.m. LOAEL(ADJ) = LOAEL (mg/cu.m) x 6.5 hours/24 hours x 5 days/7 days = 437 mg/cu.m. The LOAEL(HEC) was calculated for a gas:respiratory effect in the extrathoracic region. MVa = 0.24 cu.m/day, MVh = 20 cu.m/day, Sa (ET) = 11.6 sq.cm, Sh (ET) = 177 sq.cm. RGDR = (MVa/Sa) / (MVh/Sh) = 0.18. LOAEL(HEC) = 437 x RGDR = 79 mg/cu.m.

___I.B.2. PRINCIPAL AND SUPPORTING STUDIES (INHALATION RfC)

Foo, S., J. Jeyaratnam and D. Koh. 1990. Chronic neurobehavioral effects of toluene. Br. J. Ind. Med. 47(7): 480-484.

NTP (National Toxicology Program). 1990. Toxicology and carcinogenesis studies of toluene in F344/N rats and B6C3F1 mice (inhalation studies). NTP-TR-371. 253 p.

In humans, toluene is a known respiratory irritant with central nervous

system (CNS) effects. Because available studies could not provide subthreshold (NOAEL) concentrations for either of these effects, the LOAELs for both effects need to be considered in developing the RfC. Consequently, the study of Foo et al. (1990) was used for the CNS effects, and that of the National Toxicology Program (NTP, 1990) for the irritant effects. Because the CNS effect was judged to be a more severe and relevant endpoint, the LOAEL for this effect was used for deriving the RfC. Further, this effect is supported by a number of other occupational studies that show effects around 100 ppm.

Foo et al. (1990) conducted a cross-sectional study involving 30 exposed female workers employed at an electronic assembly plant where toluene was emitted from glue. Toluene levels reported in the study were from personal sample monitoring and reported as an 8-hour TWA, although the number of samples taken and the actual sampling period were not given. No historical exposure values were given. Co-exposure to other solvents was not addressed in the study. The exposed and control cohorts were matched for age, ethnicity, and use of medications. Members of these cohorts did not use alcohol and were nonsmokers. Medical histories were taken to eliminate any histories of central or peripheral nervous system disorders. The average number of years (+/- SD) worked by the exposed population was 5.7 +/- 3.2 and by the controls was 2.5 +/- 2.7. Exposed workers breathed toluene air levels of 88 ppm (332 mg/cu.m) as a TWA and control workers 13 ppm (49 mg/cu.m) (TWA); both of which are averages of the individual personal samples. A battery of eight neurobehavioral tests were administered to all exposed and control workers. The tests were performed midweek, before the workers reported to their stations for the day. Group means revealed statistically significant differences in 6/8 tests; all tests showed that the exposed workers performed poorly compared with the control cohort. When individual test results were linearly regressed against personal exposure concentrations, poor concentration-response relationships resulted for the six tests, with correlation coefficients ranging from 0.44 to 0.30. Irritation effects were not evaluated in this study, and no clinical signs or symptoms were reported. The paucity of exposure information, coupled with the small size of the cohort, limits the interpretation of this study, although the results were essentially confirmed in a clinical study in which the toluene concentrations were carefully controlled (Echeverria et al., 1989) at levels bracketing 88 ppm. Although the data in Echeverria et al. (1989) were generated from short-term exposures (3-7 hours over a period of 142 days), the results may be considered relevant to longer-term exposures as several studies indicate the absence of a duration-response relationship in toluene-induced symptomatology. Fornazzari et al. (1983) noted the absence of a duration-effect relationship among toluene abusers when they were segregated into neurologically impaired vs. unimpaired ($p = 0.65$). The human studies of Iregren (1982), Cherry et al. (1985), Baelum et al. (1985), and the principal study of Foo et al. (1990) all report this lack of a duration-response relationship and confirm the occurrence of CNS effects. Foo et al. (1990) indicate a LOAEL of 88 ppm toluene (332 mg/cu.m) for neurobehavioral changes from chronic exposure to toluene.

In a 2-year bioassay, Fischer 344 rats (60/sex/group) were exposed to 0, 600, or 1200 ppm (0, 2261, or 4523 mg/cu.m, respectively) toluene vapors, 6.5 hours/day, 5 days/week (duration-adjusted to 0, 437, and 875 mg/cu.m, respectively) for 103 weeks (NTP, 1990). To generate toluene vapor, the liquid material was heated, and the vapor diluted with nitrogen and mixed with the chamber ventilation air. An interim sacrifice was carried out at 15

months on control and 1200-ppm groups (10/sex/group) to conduct hematology and histopathology of the brain, liver, and kidney. Body weights were measured throughout the study. Gross necropsy and micropathology examinations were performed at the end of the study on all major organs including the nasal passage tissues (three sections), lungs, and mainstem bronchi. Mean body weights in both exposed groups were not different from controls for either sex. No exposure-related clinical signs were reported, and survival rate was similar for all groups. At the interim sacrifice, there was a mild-to-moderate degeneration in the olfactory and respiratory epithelium of the nasal cavity in 39/40 rats of the 600- and 1200-ppm groups compared with 7/20 controls. At the end of 2 years, there was a significant ($p<0.05$) increase in the incidence of erosion of the olfactory epithelium (males: 0/50, 3/50, and 8/49; females: 2/49, 11/50, and 10/50; at 0, 600, and 1200 ppm, respectively) and of degeneration of the respiratory epithelium (males: 15/50, 37/50, and 31/49; females: 29/49, 45/50, and 39/50; at 0, 600, and 1200 ppm, respectively) in the exposed animals. The females exposed to 600 and 1200 ppm also exhibited a significant increase in inflammation of the nasal mucosa (27/49, 42/50, and 41/50 at 0, 600, and 1200 ppm, respectively) and respiratory metaplasia of the olfactory epithelium (0/49, 2/50, and 6/50 at 0, 600, and 1200 ppm, respectively). A LOAEL of 600 ppm toluene was determined for the concentration-dependent increase in erosion of the olfactory epithelium in male rats and the degeneration of the respiratory epithelium in both sexes. No NOAEL could be derived from this study.

___I.B.3. UNCERTAINTY AND MODIFYING FACTORS (INHALATION RfC)

UF -- An uncertainty factor of 10 is used to account for intraspecies variability and another factor of 10 for the use of a LOAEL. An additional factor of 3 is applied for data base deficiencies, including the lack of data and well-characterized laboratory animal exposures evaluating neurotoxicity and respiratory irritation.

MF -- None

___I.B.4. ADDITIONAL STUDIES / COMMENTS (INHALATION RfC)

Toluene-induced neurotoxicity has been documented in humans over a broad spectrum of severity that correlates well with concentration. Numerous case studies on chronic toluene abusers [repeatedly exposed to greater than 30,000 ppm (113,000 mg/cu.m)] have demonstrated functional deficits of the CNS accompanied by abnormal morphology of cerebellar and cortical areas of the brain. Under acute exposure conditions [short exposures to greater than 10,000 ppm (37,690 mg/cu.m)], toluene produces CNS narcosis [American Conference of Governmental Industrial Hygienists (ACGIH), 1991]. Lower concentrations, i.e., 800-400 ppm (3015-1508 mg/cu.m), have been associated with worker complaints of CNS-related effects (ACGIH, 1991). Clinical studies

using controlled exposure to toluene have demonstrated concentration-related occurrence of complaints such as drowsiness, ataxia, visual impairment, and headache. A number of occupational studies indicate that these same effects are present in exposed worker populations at concentrations lower than 400 ppm (1508 mg/cu.m) although deficiencies in most of these studies preclude confirming this finding unequivocally. Descriptions of a number of these studies follow. The preponderence of the literature showing CNS effects and the well-known proclivity for solvents to affect CNS processes in humans leave little doubt that the brain is a principal target organ for toluene toxicity in humans.

In cases of inhalation abuse of toluene, Rosenberg et al. (1988) demonstrated diffuse cerebral, cerebellar, and brainstem atrophy in 3 of 11 toluene abusers who also had neurological abnormalities. Filley et al. (1990) were able to correlate neuropsychological impairment with the degree of white matter abnormality ($p<0.01$). Cerebellar and cortical functions were classified as impaired in 15/24 individuals who had abused toluene daily (425 +/- 366 mg/day) for extended periods (6.3 +/- 3.9 years) (Fornazzari et al., 1983). In a limited case study, Metrick and Brenner (1982) demonstrated brainstem atrophy through computerized tomographic scans and abnormal brainstem auditory-evoked potentials in 2/2 chronic toluene abusers (12-16 years of admitted, continuous abuse). These studies confirm the occurrence of severe CNS damage in response to highly abusive concentrations of toluene.

Several studies that have investigated the occurrence of neurotoxicity at lesser concentrations, such as occupational situations, have not demonstrated significant neurological or other effects. Hanninen et al. (1987) performed a battery of 11 psychological tests on 43 printing workers who had been occupationally exposed to approximately 117 ppm (441 mg/cu.m) toluene for an average of 22 years and found only mildly adverse effects in 2/11 tests. The control and exposed cohorts in this study were, however, mismatched in several areas, most notably alcohol use. Iregren (1982) examined the psychological performance of 38 printers who had been occupationally exposed to 50-150 ppm (188-565 mg/cu.m) toluene for an average of 16.3 years (range 3-32 years). No effects were seen, although the cohorts in this study were apparently matched only by age. In a cohort study, Cherry et al. (1985) attempted to better match the control and exposed cohorts and considered alcohol use. Although no differences between the cohorts were statistically significant, the exposed workers performed worse than the nonexposed workers on 10/13 psychological tests. The 52 workers in this study were not, however, rigorously matched, and the concentrations listed in the study ranged up to greater than 500 ppm (1884 mg/cu.m). The cohorts in the study of Foo et al. (1990) were well matched for a number of confounders, including alcohol use, and statistically significant psychological effects were seen.

In the occupational study conducted by Yin et al. (1987), 94 solvent workers (38 men and 56 women; average employment duration, 6.8 years) and 138 controls (48 men and 90 women) were examined for exposure using diffusion dosimeters, subjective symptoms by questionnaire, hematology, and urinalysis. Exposure concentration (7-hour mean TWA) in the workers was estimated at 42.8 ppm (161 mg/cu.m) toluene with a maximum measurement of 123 ppm (464 mg/cu.m). Workers were co-exposed to 1.3 ppm benzene. No exposure-related effects were noted in any of the biochemical tests examined. In considering the prevalence of subjective symptoms (sore throat, headaches, and dizziness) workers were subgrouped into low (6-39 ppm, n = 28) and high (40-123 ppm, n = 29)

categories. Although the prevalence of subjective symptoms was significantly higher in the exposed workers compared with the control cohort ($p<0.01$), a concentration-response relationship was not discernable among the groups. No other treatment-related effects were reported. The study was limited because the exposed and unexposed groups were not matched to control for confounding effects (e.g., age, smoking, alcohol consumption, exposure duration). Based on these results, exposure to an average of approximately 42.8 ppm toluene produced no biochemical abnormalities, although neither respiratory irritation nor psychological performance was directly evaluated in these workers.

In the occupational study by Lee et al. (1988), prevalence of subjective symptoms was categorized with respect to exposure levels. The study population (193 women and 65 controls) completed a questionnaire. The exposures were reported as 8-hour TWAs, and workers were grouped in exposure categories of nonexposed, 1-50 ppm, 51-100 ppm, 101-150 ppm, and more than 151 ppm (duration of exposures was not reported). A concentration-dependent increase in prevalence was reported for 25/67 symptoms with increases in complaints over controls occurring at around 100 ppm (348 mg/cu.m). Similar to the Yin et al. study (1987) reported above, symptomatology included headaches, sore throats, and dizziness. Although an effect level in humans of around 100 ppm is indicated by this study, no objective measures of toxicity were examined.

A number of acute human studies have focused on toluene effects. In general, these studies corroborate subjective CNS effects such as headaches and dizziness reported in other longer-term occupational studies (Yin et al., 1987; Lee et al., 1988) and also document irritation effects. The study of Echeverria et al. (1989) correlates the occurrence of these subjective effects with substantial neurological symptoms.

Forty-two college students (21 female and 21 male) were exposed to 0, 74 ppm (279 mg/cu.m), or 151 ppm (569 mg/cu.m) toluene for 7 hours over 3 days (Echeverria et al., 1989). This exposure sequence was repeated for a total of 42 exposures over a 3-month period. The odor of toluene was masked. A battery of performance tests was administered to each participant prior to starting the exposures and again at 4 and 7 hours during the exposure; the initial test served as a control for those tests performed during the exposure. A 5-10% decrement in performance was considered significant if consistent with a linear trend. Test results for visual perception differed from control values for both exposure levels. Results of a manual dexterity test differed from control values at the higher but not the lower exposure level. Psychomotor test results were unaffected by toluene exposure. Subjective symptomatology increased with exposure with increasing numbers of complaints of eye irritation, headache, and somnolence. A NOAEL of 74 ppm (279 mg/cu.m) is indicated for these results. The duration-adjusted value is 122 mg/cu.m for these acute effects.

Andersen et al. (1983) exposed 16 subjects (average age of 24 years) to 0, 10, 40, or 100 ppm (0, 38, 151, or 377 mg/cu.m) toluene for 6 hours on each of 4 consecutive days. Individuals were tested for nasal mucous flow, lung function, subjective response, and psychometric performance. At 100 ppm, irritation was experienced in the eyes and nose, but no effect on nasal mucous flow or lung function was observed. The subjects frequently reported headaches, dizziness, and a feeling of intoxication. These effects were not reported by the 10- or 40-ppm exposure groups. No effects were seen in

performance tests. This study indicates an effect level of 100 ppm, and a NOAEL of 40 ppm (151 mg/cu.m).

The acute study by Baelum et al. (1990) evaluated 32 males and 39 females exposed to 0 or 100 ppm (0 or 377 mg/cu.m), or to varying exposures of 50-300 ppm (188-1131 mg/cu.m) (TWA = 102 ppm), for 7 hours. Volunteers exercised on an ergometer cycle for 3 periods of 15 minutes each during the exposure. No significant differences were found in the performances between the exposed and control groups in a battery of tests for performance, visual attention, and reaction times. Exposed subjects reported an increase over nonexposed subjects ($p<0.1$) in nose and lower respiratory irritation, feelings of intoxication, dizziness, increased coughing, and headaches. Differences were not noted between the group exposed to a constant level (100 ppm) and the group exposed to the same TWA, but with peaks of up to 300 ppm.

Baelum et al. (1985) investigated the effects of a 6.5-hour toluene exposure to 43 printers with a long-term occupational exposure to a mixture of solvents including toluene and 43 controls with no history of exposure to solvents or other chemicals. The duration of employment for the workers ranged from 9-25 years. Each individual was exposed only once to either 0 or 100 ppm (0 or 377 mg/cu.m) toluene during a 6.5-hour exposure period, preceded by a 1-hour acclimatization period. These subjects were then subgrouped into printers exposed to toluene (n = 20), printers exposed to air (n = 23), controls exposed to toluene (n = 21), and controls exposed to air (n = 22). All subjects carried out a battery of tests for psychometric performance, visual perception, and vigilance evaluation. Both printers and controls complained of nasal and eye irritation, unacceptable air quality, and unacceptable odor level during the toluene exposure. Signs of neurotoxicity, including moderate fatigue, sleepiness, headaches, and a feeling of intoxication, were likewise similarly reported for both groups. A significant decrease in performance was found for the pegboard visual motor function test in the exposed printers, but not in the controls exposed to 100 ppm toluene. A decrease in psychometric performance, primarily in visual perception and accuracy, was observed in toluene-exposed individuals. Acute exposure to toluene resulted in a lower performance in 4/10 tests conducted, 3 of these 4 evaluated visual perception. The most profound difference between subjects exposed to 100 ppm toluene and those exposed to clean air was observed in the color discrimination test; this difference was seen in both exposed vs. nonexposed printers and exposed vs. nonexposed controls. This study indicates that little tolerance develops to the irritative and central effects in humans exposed to toluene and that 100 ppm (377 mg/cu.m) is the effect level for these symptoms.

Von Oettingen et al. (1942) exposed 3 humans to 100 or 200 ppm (377 or 754 mg/cu.m) toluene vapors for 8 hours. At 200 ppm, the subjects experienced muscular weakness, confusion, impaired coordination, and dilated pupils, with after-effects including fatigue, general confusion, and moderate insomnia. In 1 subject exposed to 100 ppm toluene, moderate fatigue, sleepiness, and headaches were reported.

Hepatotoxicity has also been examined as a toxicologic endpoint of toluene exposure in humans. Fornazzari et al. (1983) described moderate elevation of serum AP levels in 13/24 (and SGOT in 7/24) toluene abusers upon admission to a clinic. These elevated levels were normal after 2 weeks of solvent abstinence, although the accompanying CNS effects were only minimally

improved. In a cross-sectional study of 181 printing workers in which toluene exposures were less than 200 mg/cu.m, no adverse effects were apparent as judged from serum liver enzymes (Boewer et al., 1988). In another cross-sectional occupational study conducted by Guzelian et al. (1988) that involved 289 printing factory employees, 8 workers were found who had an increase described as "marked" in the ratio of ALT/AST enzyme serum activity. Biopsies revealed mild pericentral fatty livers in each of the eight cases. Based on environmental data (probably area monitors) the levels of toluene to which these workers were exposed was less than 200 mg/cu.m., 2-8 hours/day.

Fischer 344 rats (120/sex/group) inhaled 0, 30, 100, or 300 ppm (0, 113, 377, or 1130 mg/cu.m, respectively) toluene (99.9% purity), 6 hours/day, 5 days/week (duration-adjusted to 0, 20, 67, or 202 mg/cu.m, respectively) for 106 weeks (CIIT, 1980; Gibson and Hardisty, 1983). Vapor, generated by bubbling clean air through toluene, was passed through the air supply duct and mixed with air by turbulent flow to produce the desired concentration. Hematology, blood chemistry, and urinalysis were conducted in all groups at 6 (5/sex), 17 (5/sex), 18 (10-20/sex), and 24 months (10/sex). Histopathology was evaluated only in the control and 300-ppm groups at 6 (5/sex), 12 (5/sex), and 18 months (20/sex). At 24 months, histopathological examinations were conducted in organs of all surviving animals, including the respiratory system and sections through the nasal turbinates (number not indicated). No treatment-related non-neoplastic effects were observed in the exposed animals. Although the male rats exposed to 300 ppm had a significant increase in body weight compared to controls, no concentration-response was evident. At the end of the exposure period, the female rats exposed to 100 or 300 ppm exhibited a slight but significant reduction in hematocrit; an increase in the mean corpuscular hemoglobin concentration was also noted but only in the females exposed to 300 ppm. The highest concentration examined in this study, 300 ppm, is designated as a NOAEL for toxicity remote from the respiratory tract in rats. CIIT (1980) reported that the technical and raw data were not audited by their quality assurance group during the study period, although CIIT did conduct a quality assessment procedure to review the data. The available pathology reports containing these data indicate that at least the lower respiratory tract was examined. Communication with the testing sponsor has provided information indicating that only one section was examined from the nasal cavity of these test animals. It is not clear whether this single section would have been sufficient to elucidate the areas of lesions noted in the NTP (1990) study. Consequently, the designation of the 300-ppm exposure level as a NOAEL for respiratory lesions (see NTP,1990) is problematic.

Fischer 344/N rats (10/sex/group) were exposed to toluene vapors at 0, 100, 625, 1250, 2500, and 3000 ppm (0, 377, 2355, 4711, 9422, and 11,307 mg/cu.m, respectively) 6.5 hours/day, 5 days/week (duration-adjusted to 0, 73, 455, 911, 1823, and 2187 mg/cu.m, respectively) for 15 weeks (NTP, 1990). Organ weights were measured and histological examinations were performed only on controls, 2500- and 3000-ppm groups, and animals that died before the end of the study. Eight of 10 males exposed to 3000 ppm died, all during the 2nd exposure week. No females died at any exposure level. Compared to the controls, final body weights were 15 and 25% lower in the males and 15 and 14% lower in the females of the 2500- and 3000-ppm groups, respectively. There was a concentration-related increase in the relative liver weight, significant at 1250, 2500, and 3000 ppm in males and at 2500 and 3000 ppm in females. The relative weights of the heart, lung, kidney, and right testis were also significantly elevated in the 2500- and 3000-ppm animals compared to those of

the controls, although no histopathology was observed in any exposure group. Toxic effects noted in a concurrently conducted gavage study (urinary bladder hemorrhages in the two highest exposure groups) were not noted in this subchronic inhalation study. A LOAEL of 2500 ppm [LOAEL(HEC) = 1823 mg/cu.m] was determined for the decrease in body weight gain in both males and females, and the NOAEL for this effect was 1250 ppm [NOAEL(HEC) = 911 mg/cu.m].

Toluene has been suspected to cause congenital defects in infants born to mothers who were exposed to or who abused toluene during pregnancy. In a case report study, Hersh et al. (1985) describes clinical and morphometric characteristics common to 3 children whose mothers had abused toluene (but apparently not alcohol or any other substance) for a period of 4-5 years including during their pregnancies with the affected children. Clinical findings common to these three children included microcephaly, CNS dysfunction, attention deficits, and developmental delay/mental deficiency. Phenotypic similarities included a small midface, deep-set eyes, micrognathia (smallness of the jaws), and blunting of the fingertips. A retrospective cohort study was conducted by McDonald et al. (1987) who examined the history of exposure to chemicals of 301 women who had recently given birth to an infant with an important congenital defect. An identical number of women (referents) who had given birth to normal children were matched with respect to age, employment (hours/week), date of delivery, and educational level. In initial matched-pair analysis, chemical exposure was higher in the cases than in the referents (63 cases:47 referents) due to excess cardiac and miscellaneous defects. In further analysis by chemical categories, only exposure to aromatic solvents showed a clear excess of defects, mostly in the urinary tract. Details of these cases (n = 19) showed that toluene was identified as the solvent in 11 of these cases.

Hudak and Ungvary (1978) exposed three groups of pregnant CFY rats to toluene during different periods of gestation and for different durations of exposure. Two of the groups had their own control group exposed to air only and matched for period and daily duration. The first of these (n = 19) was exposed to 1500 mg/cu.m for 24 hours/day during gestational days 9 to 14. Two dams died during these exposures. No details on the deaths are given but no other maternal toxicity was observed. Fetotoxicity was also in evidence as sternebral alterations (6% vs. 1% in controls), extra ribs (22% vs. 0% in controls), and the presence of fetuses with missing tails (2/213, none observed in 315 controls) were recorded. Under these exposure conditions, 1500 mg/cu.m is a LOAEL for fetotoxicity and a frank effect level (FEL) for maternal toxicity. The second group (n = 14) received this same concentration continuously but on days 1-8 of gestation. Five dams died under these exposure conditions although toxicity parameters of the surviving dams were identical with the controls from the first group (gestational days 9-14). Slight hydrocephaly was noted in 4 fetuses (all from the same litter), and 17% growth retardation was noted vs. 7% in the controls. Thus these exposure conditions are a FEL for maternal toxicity and a LOAEL for fetotoxicity. A third group was exposed to 1000 mg/cu.m for 8 hours/day from the 1st to the 21st day of gestation. No maternal deaths or toxicity occurred. Minor skeletal retardation was present in the exposed fetuses at a higher incidence rate (25%) than in concurrent controls (0%). These results indicate that 1000 mg/cu.m is a LOAEL for developmental effects under these exposure conditions. This concentration is also a NOAEL for maternal effects. These workers also exposed groups of pregnant CFLP mice (n = 11-15) to either air or 1500 or 500 mg/cu.m toluene continuously during days 6-13 of pregnancy. All mice exposed to the

high concentration died within 24 hours of the beginning of exposure. No dams died in the lower exposure group. In this group, the average fetal weight decreased to 0.96 g from the average control weight of 1.07 g, and the percentage of weight-retarded fetuses (less than 0.9 g) increased to 27.6% from 6.5% in the controls. No difference in incidence of skeletal malformations or anomalies was noted between these and control fetuses. For mice, 1500 mg/cu.m is an FEL and 500 mg/cu.m is a mild LOAEL. Since duration adjustment is not performed for developmental effects, this concentration is also the LOAEL(HEC).

B6C3F1 mice (60/sex/group) were exposed to 0, 120, 600, or 1200 ppm (0, 452, 2261, or 4523 mg/cu.m, respectively) toluene 6.5 hours/day, 5 days/week (duration-adjusted to 0, 87, 47, and 875 mg/cu.m, respectively) for 2 years (NTP, 1990). Mean body weights were not significantly different among groups and no treatment-related clinical signs were observed. Deaths (moribund and natural) occurred in all exposure groups but were not related to exposure and were not greater than the control rates. An excess incidence of non-neoplastic inflammatory lesions of the urinary and genital system was observed in all the groups of male mice. At the 15-month interim sacrifice, minimal hyperplasia in the bronchial epithelium was observed in 4/10 females exposed to 1200 ppm. At the end of the study, there was a concentration-dependent increase in the incidence of splenic pigmentation in the exposed males (9/60, 11/60, and 18/59 at 120, 600, and 1200 ppm, respectively) compared to controls (4/60). In the females, the incidence was 37/50, 33/50, 34/49, and 28/47 at 0, 120, 600, and 1200 ppm, respectively. The occurrence of endometrial hyperplasia was present in 14% of the animals exposed to the highest concentration but only in 4% in the low-exposure groups and controls. No differences were noted between the exposed and control mice of either sex in the incidence of degeneration of either the olfactory or respiratory epithelium. No other non-neoplastic lesions were observed in exposed mice. As no adverse effects were noted in this study, the highest concentration, 1200 ppm was designated as a NOAEL in mice for this chronic study [NOAEL(HEC) = 875 mg/cu.m].

Sprague-Dawley rats (15/sex/group) were exposed to cumulative mean exposures of 0, 100, or 1481 ppm (0, 377, or 5653 mg/cu.m) toluene vapors, 6 hours/day, 5 days/week (duration-adjusted to 0, 67, and 1009 mg/cu.m, respectively) for 26 weeks (API, 1981). On weeks 9, 18, and 27, neurohistopathological examinations were conducted in 3-5 rats/sex/group. Hematology, clinical chemistry, and urinalysis parameters were evaluated after 13 and 26 weeks of exposure. Body weights were measured weekly. No significant treatment-related effects were reported. Therefore, a NOAEL of 1481 ppm [NOAEL(HEC) = 1009 mg/cu.m] toluene was determined for systemic effects in rats. The study was limited because there were no other neurohistopathological examinations or organ weight measurements conducted on the animals.

Inhalation exposure to toluene has been shown to result in irreversible high-frequency hearing loss in rats. Pryor et al. (1984) exposed young male Fischer 344 rats to a variety of exposure concentrations and durations. Hearing loss was evaluated by a behavioral technique (avoidance response elicited to an auditory signal) or brainstem auditory-evoked responses (elicited by tone pips of differing loudness and frequency and detected by subdural scalp electrodes). Hearing loss, as measured by both techniques, was observed after as few as 2 weeks exposure to 1000 ppm toluene for 14 hours/day. Lower concentrations of 700 ppm for 14 hours/day were without

effect after 16 weeks of exposure. Intermittent exposure to 3000 ppm for 30 minutes/hour for 8 hours/day caused hearing loss within 2 weeks, whereas a similar exposure schedule for only 4 hours/day was without effect after 9 weeks. These data define a NOAEL for hearing loss in rats of 700 ppm [NOAEL(HEC) = 2638 mg/cu.m]. The duration-adjusted HEC (assumed 5 days/week) would be 14/24 hours x 5/7 days = 1100 mg/cu.m. Although these results clearly document hearing loss in young adult rats, their direct significance to humans remains unclear. Among chronic toluene abusers there is only a single report of adverse effects on hearing; Metrick and Brenner (1982) claimed that the abnormal auditory-evoked potentials recorded in two chronic toluene abusers was evidence of brainstem abnormalities.

Pregnant Wistar rats and hamsters (group size not indicated) inhaled 0 or 800 mg/cu.m toluene vapors 6 hours/day on gestational days 14-20 (rats) or gestational days 6 to 11 (hamsters) (DaSilva et al., 1990). In the exposed rats, there was a significant ($p<0.05$) increase in the number of litters with one or more low birth weight pups (less than 4.9 g), from 10% in the controls to 54% in the exposed dams. A decrease ($p<0.05$) in the number of live pups at birth was also noted in the litters of exposed dams. No evaluation of malformations or anomalies was performed. The neurobehavioral development of the offspring of the exposed rats was assessed using tests of spontaneous alternation, rim escape, and avoidance responses. The only effect noted in the rats, a shortened first trial latency in choosing one side of a maze, was minimal and its significance unclear. No comparable reproductive deficits occurred in the exposed hamsters. The only effect noted in the neurobehavioral tests of the hamster offspring was an equivocal effect in rota-rod performance. No neurobehavioral effect levels were designated from this study, although it appears that the rat developmental processes are more sensitive than those of the hamster, exhibiting adverse effects at 800 mg/cu.m.

Ungvary and Tatrai (1985) exposed New Zealand rabbits (8-10/group) to 0, 500, or 1000 mg/cu.m toluene, 24 hours/day, on gestational days 7-20, and CFLP mice (15 females/group) to 0, 500, 1000, or 1500 mg/cu.m toluene, also continuously, on gestational days 6-15. The control groups consisted of 115 mice and 60 rabbits. All the female mice exposed to 1500 mg/cu.m died. In the mice exposed to 1000 mg/cu.m, there was an increase in fetuses with retarded weight (29%, level of retardation not indicated) and in fetuses with skeletal retardation (12%) compared to 7% and 5%, respectively, in the controls, which did not differ from the animals exposed to 500 mg/cu.m. Of the 8 pregnant rabbits exposed to 1000 mg/cu.m, 2 died, 4 had spontaneous abortions, and the remaining 2 had total litter resorption. No deaths occurred in the 10 rabbits exposed to 500 mg/cu.m but 1/10 rabbits had a spontaneous abortion (as compared to 0/60 reported for the controls). A NOAEL(HEC) of 500 mg/cu.m toluene was determined for reproductive effects in mice. For rabbits, the 500 mg/cu.m concentration is designated as a LOAEL. These results indicate that pregnant mice may be a sensitive population to the effects of toluene.

Pregnant Charles River CD-1 mice (15-16 females/group) inhaled filtered air or 200 or 400 ppm (754 and 1508 mg/cu.m) toluene 7 hours/day on gestational days 7-16 (Courtney et al., 1986). The relative liver weight in the exposed dams was reported to be significantly lower in the two exposed groups compared to the controls, although no data were presented. A statistically significant increase in lactate dehydrogenase activity in the brain of the dams exposed to 400 ppm was also reported. The exposed pregnant

mice did not exhibit any significant differences in the number of implantation sites, number of live fetuses, fetal deaths, or fetal body weight compared to the control values. A statistically significant increase over controls in the incidence (both per litter and per fetus) of enlarged renal pelves was noted in dams exposed to 200 ppm but not 400 ppm. A statistically significant alteration from controls in the rib profile (percentage of fetuses with 1 or 2 additional/fewer ribs) was reported for fetuses from dams exposed to 400 ppm but not 200 ppm. The toxicological significance of this finding is not clear. As no clearly significant toxicological effects were observed, the highest concentration used, 400 ppm [NOAEL(HEC) = 1508 mg/cu.m] is designated as a NOAEL for reproductive and developmental effects in mice.

A 2-generation inhalation reproductive study was conducted in CD rats (10-40 males, 20-80 females/group) (API, 1985). Animals were exposed by whole-body inhalation to toluene at 0, 100, 500, or 2000 ppm (0, 377, 1885, or 7538 mg/cu.m, respectively) 6 hours/day, 7 days/week for 80 days and a 15-day mating period. The mated females were then exposed to the same concentrations during days 1-20 of gestation and days 5-20 of lactation. After weaning, the pups in this generation (F1) were exposed 80 times and then randomly mated with members of the same exposure group (2 females/1 male) to produce the second generation (F2). Mean male body weights were slightly reduced (maximum of 10%) in the first 2 weeks of the exposure in the animals exposed to 500 and 2000 ppm, although the size of the reduction was not related to exposure. No differences were observed in male or female fertility indices, length of gestation, mean numbers of viable and nonviable pups at birth, or pup survival indices during lactation. No abnormal histopathology was noted in organs examined. A significant decrease ($p<0.05$) in weight relative to controls was observed in the first generation offspring. The decrease was maintained throughout the lactation period in the pups from dams exposed to the highest exposure and in those from the ancillary group in which females exposed to the 2000 ppm concentration were mated with males having no exposure. No data were available in the report about the F2 generation. Based on the effects on the pups of the first generation (F1), a LOAEL of 2000 ppm [LOAEL(HEC) = 7538 mg/cu.m] is designated, the NOAEL being 500 ppm [NOAEL(HEC) = 1885 mg/cu.m].

I.B.5. CONFIDENCE IN THE INHALATION RfC

Study -- Medium
Data Base -- Medium
RfC -- Medium

The study of Foo et al. (1990) indicates adverse neurological effects of toluene in a small worker population. These effects are consistent with more severe CNS effects occurring at abusive concentrations of toluene and could not have been confounded by alcohol as the control and exposed populations did not use alcohol. However, the paucity of exposure information and identification of only a LOAEL is not sufficient to warrant a higher confidence than medium for this study.

Other studies indicate that irritation may occur at around the same concentration, 100 ppm (Baelum et al., 1985; Echeverria et al., 1989). In

regard to this effect, the NTP (1990) rat chronic inhalation study was well conducted, established the rat as the most sensitive species, examined an adequate number of animals, and performed histopathology on all major organs, including the brain and the respiratory tract. The sensitive endpoint was the concentration-dependent degeneration of the nasal epithelium characterized by the erosion of the olfactory epithelium and degeneration of the respiratory epithelium in male rats. The NTP study is also given medium confidence, however, as it did not establish a NOAEL.

Although this data base has a complement of chronic laboratory animal studies, long-term data in humans are not available for either the neurotoxicity or irritation endpoints. The reproductive/developmental studies in three species were not comprehensive in endpoint evaluation but do identify the rabbit as the most sensitive species. The data base is thus given a medium confidence rating. A medium confidence rating for the RfC follows.

___I.B.6. EPA DOCUMENTATION AND REVIEW OF THE INHALATION RfC

Source Document -- This assessment is not presented in any existing U.S. EPA document.

Other EPA Documentation -- U.S. EPA, 1984, 1985

Agency Work Group Review -- 04/21/1988, 05/26/1988, 02/16/1989, 03/21/1989, 05/18/1989,
08/15/1991, 12/11/1991

Verification Date -- 05/18/1989, 12/11/1991

___I.B.7. EPA CONTACTS (INHALATION RfC)

Please contact the Risk Information Hotline for all questions concerning this assessment or IRIS, in general, at (513)569-7254 (phone), (513)569-7159 (FAX) or RIH.IRIS@EPAMAIL.EPA.GOV (internet address).

_II. CARCINOGENICITY ASSESSMENT FOR LIFETIME EXPOSURE

Substance Name -- Toluene

CASRN -- 108-88-3
Last Revised -- 02/01/1994

Section II provides information on three aspects of the carcinogenic assessment for the substance in question; the weight-of-evidence judgment of the likelihood that the substance is a human carcinogen, and quantitative estimates of risk from oral exposure and from inhalation exposure. The quantitative risk estimates are presented in three ways. The slope factor is the result of application of a low-dose extrapolation procedure and is presented as the risk per (mg/kg)/day. The unit risk is the quantitative estimate in terms of either risk per ug/L drinking water or risk per ug/cu.m air breathed. The third form in which risk is presented is a drinking water or air concentration providing cancer risks of 1 in 10,000, 1 in 100,000 or 1 in 1,000,000. The rationale and methods used to develop the carcinogenicity information in IRIS are described in The Risk Assessment Guidelines of 1986 (EPA/600/8-87/045) and in the IRIS Background Document. IRIS summaries developed since the publication of EPA's more recent Proposed Guidelines for Carcinogen Risk Assessment also utilize those Guidelines where indicated (Federal Register 61(79):17960-18011, April 23, 1996). Users are referred to Section I of this IRIS file for information on long-term toxic effects other than carcinogenicity.

__II.A. EVIDENCE FOR CLASSIFICATION AS TO HUMAN CARCINOGENICITY

___II.A.1. WEIGHT-OF-EVIDENCE CLASSIFICATION

Classification -- D; not classified

Basis -- No human data and inadequate animal data. Toluene did not produce positive results in the majority of genotoxic assays.

___II.A.2. HUMAN CARCINOGENICITY DATA

None.

___II.A.3. ANIMAL CARCINOGENICITY DATA

A chronic (106-week) bioassay of toluene in F344 rats of both sexes

reported no carcinogenic responses (CIIT, 1980). A total of 960 rats were exposed by inhalation for 6 hours/day, 5 days/week to toluene at 0, 30, 100, or 300 ppm. Groups of 20/sex/dose were sacrificed at 18 months. Gross and microscopic examination of tissues and organs identified no increase in neoplastic tissue or tumor masses among treated rats when compared with controls. The study is considered inadequate because the highest dose administered was well below the MTD for toluene and because of the high incidence of lesions and pathological changes in the control animals.

Several studies have examined the carcinogenicity of toluene following repeated dermal applications. Toluene (dose not reported) applied to shaved interscapular skin of 54 male mice (strains A/He, C3HeB, SWR) throughout their lifetime (3 times weekly) produced no carcinogen1c response (Poel, 1963). One drop of toluene (about 6 mL) applied to the dorsal skin of 20 random-bred albino mice twice weekly for 50 weeks caused no skin papillomas or carcinomas after a 1-year latency period was allowed (Coombs et al., 1973). No increase in the incidence of skin or systemic tumors was demonstrated in male or female mice of three strains (CF, C3H, or CBaH) when toluene was applied to the back of 25 mice of each sex of each strain at 0.05-0.1 mL/mouse, twice weekly for 56 weeks (Doak et al., 1976). One skin papilloma and a single skin carcinoma were reported among a group of 30 mice treated dermally with one drop of 0.2% (w/v) solution toluene twice weekly, administered from droppers delivering 16-20 uL per drop for 72 weeks (Lijinsky and Garcia, 1972). It is not reported whether evaporation of toluene from the skin was prevented during these studies.

II.A.4. SUPPORTING DATA FOR CARCINOGENICITY

Toluene was found to be nonmutagenic in reverse mutation assays with S. typhimurium (Mortelmans and Riccio, 1980; Nestmann et al., 1980; Bos et al., 1981; Litton Bionetics, Inc., 1981; Snow et al., 1981) and E. coli (Mortelmans and Riccio, 1980), with and without metabolic activation. Toluene did not induce mitotic gene conversion (Litton Bionetics, Inc., 1981; Mortelmans and Riccio, 1980) or mitotic crossing over (Mortelmans and Riccio, 1980) in S. cerevisiae. Although Litton Bionetics, Inc. (1981) reported that toluene did not cause increased chromosomal aberrations in bone marrow cells, several Russian studies (Dobrokhotov, 1972; Lyapkalo, 1973) report toluene as effective in causing chromosal damage in bone marrow cells of rats. There was no evidence of chromosomal aberrations in blood lymphocytes of workers exposed to toluene only (Maki-Paakkanen et al., 1980; Forni et al., 1971), although a slight increase was noted in workers exposed to toluene and benzene (Forni et al., 1971; Funes-Craviota et al., 1977). This finding is supported by studies of cultured human lymphocytes exposed to toluene in vitro; no elevation of chromosomal aberrations or sister chromatid exchanges was observed (Gerner-Smidt and Friedrich, 1978).

__II.B. QUANTITATIVE ESTIMATE OF CARCINOGENIC RISK FROM ORAL EXPOSURE

Not available.

__II.C. QUANTITATIVE ESTIMATE OF CARCINOGENIC RISK FROM INHALATION EXPOSURE

Not available.

__II.D. EPA DOCUMENTATION, REVIEW, AND CONTACTS (CARCINOGENICITY ASSESSMENT)

___II.D.1. EPA DOCUMENTATION

Source Document -- U.S. EPA, 1987

The values in the 1987 Drinking Water Criteria Document for Toluene have received peer and administrative review.

___II.D.2. REVIEW (CARCINOGENICITY ASSESSMENT)

Agency Work Group Review -- 09/15/1987

Verification Date -- 09/15/1987

___II.D.3. U.S. EPA CONTACTS (CARCINOGENICITY ASSESSMENT)

Please contact the Risk Information Hotline for all questions concerning this assessment or IRIS, in general, at (513)569-7254 (phone), (513)569-7159 (FAX) or RIH.IRIS@EPAMAIL.EPA.GOV (internet address).

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CASRN -- 108-88-3
Last Revised -- 08/01/1992

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_VII. REVISION HISTORY

Substance Name -- Toluene
CASRN -- 108-88-3

Date	Section	Description
03/01/1988	I.A.4.	Text revised
09/07/1988	II.	Carcinogen summary on-line
02/01/1989	II.D.3.	Secondary contact's phone number corrected
07/01/1989	I.B.	Inhalation RfD now under review
03/01/1990	VI.	Bibliography on-line
04/01/1990	VI.C.	Combs et al., 1973 citation corrected
06/01/1990	IV.A.1.	Area code for EPA contact corrected
06/01/1990	IV.F.1.	EPA contact changed
07/01/1990	I.A.	Withdrawn; new RfD verified (in preparation)
07/01/1990	VI.A.	Oral RfD references withdrawn
08/01/1990	I.A.	Oral RfD summary replaced; RfD changed
08/01/1990	II.	Text edited
08/01/1990	VI.A.	Oral RfD references revised
09/01/1990	III.A.	Health Advisory on-line
09/01/1990	VI.D.	Health Advisory references added
08/01/1991	VI.C.	Litton Bionetics, Inc., 1981 reference title clarified
01/01/1992	IV.	Regulatory actions updated
04/01/1992	IV.A.1.	CAA regulatory action withdrawn
08/01/1992	I.B.	Inhalation RfC on-line
08/01/1992	VI.B.	Inhalation references on-line
02/01/1994	II.D.3.	Secondary contact's phone number changed
04/01/1994	I.A.7.	Primary contact changed
04/01/1997	III.,IV., V.	Drinking Water Health Advisories, EPA Regulatory Actions, and Supplementary Data were removed from IRIS on or before April 1997. IRIS users were directed to the appropriate EPA Program Offices for this information.

VIII. SYNONYMS

Substance Name -- Toluene
CASRN -- 108-88-3
Last Revised -- 01/31/1987

108-88-3
ANTISAL 1a
BENZENE, METHYL
METHACIDE
METHYL-BENZENE

METHYLBENZOL
NCI-C07272
PHENYL-METHANE
RCRA WASTE NUMBER U220
TOLUEEN
TOLUEN
Toluene
TOLUOL
TOLUOLO
TOLU-SOL
UN 1294
.

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Last updated: **5 May 1998**
URL: http://www.epa.gov/iris/subst/0118.htm

Drinking Water and Health

As part of the Drinking Water and Health pages, this fact sheet is part of a larger publication:

National Primary Drinking Water Regulations

Consumer Factsheet on: TOLUENE

This is a factsheet about a chemical that may be found in some public or private drinking water supplies. It may cause health problems if found in amounts greater than the health standard set by the United States Environmental Protection Agency (EPA).

What is Toluene and how is it used?

Toluene is an organic liquid with a sweet, benzene-like odor. The largest chemical use for toluene is to make benzene and urethane.

The list of trade names given below may help you find out whether you are using this chemical at home or work.

Trade Names and Synonyms:

Methylbenzene
Methacide
Phenylmethane
Toluol
Antisal 1A

Why is Toluene being Regulated?

In 1974, Congress passed the Safe Drinking Water Act. This law requires EPA to determine safe levels of chemicals in drinking water which do or may cause health problems. These non-enforceable levels, based solely on possible health risks and exposure, are called Maximum Contaminant Level Goals.

The MCLG for toluene has been set at 1 parts per million (ppm) because EPA believes this level of protection would not cause any of the potential health problems described below.

Based on this MCLG, EPA has set an enforceable standard called a Maximum Contaminant Level (MCL). MCLs are set as close to the MCLGs as possible, considering the ability of public water systems to detect and remove contaminants using suitable treatment technologies.

The MCL has also been set at 1 ppm because EPA believes, given present technology and resources, this is the lowest level to which water systems can reasonably be required to remove this contaminant should it occur in drinking water.

These drinking water standards and the regulations for ensuring these standards are met, are called National Primary Drinking Water Regulations. All public water supplies must abide by these regulations.

What are the Health Effects?

Short-term: EPA has found toluene to potentially cause the following health effects when people are exposed to it at levels above the MCL for relatively short periods of time: minor nervous system disorders such as fatigue, nausea, weakness, confusion.

Long-term: Toluene has the potential to cause the following effects from a lifetime exposure at levels above the MCL: more pronounced nervous disorders such as spasms, tremors, impairment of speech, hearing, vision, memory, coordination; liver and kidney damage.

How much Toluene is produced and released to the environment?

Production of toluene was 6.4 billion lbs in 1993. It is released into the atmosphere principally from the volatilization of petroleum fuels and toluene-based solvents and thinners and from motor vehicle exhaust. It is also released in wastewaters or by spills on land during the storage, transport and disposal of fuels and oils.

From 1987 to 1993, according to EPA's Toxic Chemical Release Inventory, toluene releases to land and water totalled over 4 million lbs., primarily from petroleum refining industries. The largest releases occurred in Texas and California. The largest releases directly to water occurred in Connecticut and West Virginia.

What happens to Toluene when it is released to the environment?

Toluene released to soil will be lost by evaporation from near-surface soil and by leaching to the groundwater. Its breakdown by soil microbes is slow. Toluene evaporates within a few hours when released to water, and it has little tendency to accumulate in aquatic life.

How will Toluene be Detected in and Removed from My Drinking Water?

The regulation for toluene became effective in 1992. Between 1993 and 1995, EPA required your water supplier to collect water samples every 3 months for one year and analyze them to find out if toluene is present above 0.5 ppb. If it is present above this level, the system must continue to monitor this contaminant.

If contaminant levels are found to be consistently above the MCL, your water supplier must take steps to reduce the amount of toluene so that it is consistently below that level. The following treatment methods have been approved by EPA for removing toluene: Granular activated charcoal in combination with Packed Tower Aeration.

How will I know if Toluene is in my drinking water?

If the levels of toluene exceed the MCL, 1 ppm, the system must notify the public via newspapers, radio, TV and other means. Additional actions, such as providing alternative drinking water supplies, may be required to prevent serious risks to public health.

Drinking Water Standards:

Mclg: 1 ppm

Mcl: 1 ppm

Toluene Releases to Water and Land, 1987 to 1993 (in pounds):

		Water	Land
TOTALS* (in pounds)		**732,310**	**3,672,041**
Top Ten States*			
TX	16,285	969,210	
CA	0	930,000	
CT	316,068	0	
OK	0	287,000	
VA	27,500	216,000	
VI	2,970	191,504	
IL	56	180,824	
MI	0	129,226	
WV	117,523	1,377	
SC	6,000	89,578	
Major Industries*			
Petroleum refining		227,196	2,580,941
Medicinals, botanicals		301,585	1,108
Petroleum/coal prods.		38,856	287,000
Misc Ind. Chemicals		179,576	107,159
Gaskets, sealing devices		4,002	216,000
Wood office furniture		0	129,226
Plastics, resins		57,661	39,139
Wood home furniture		30,000	65,444
Paints, allied products		5,927	88,024

* Water/Land totals only include facilities with releases greater than 10,000 lbs.

Learn more about your drinking water!

EPA strongly encourages people to learn more about their drinking water, and to support local efforts to protect and upgrade the supply of safe drinking water. Your water bill or telephone books government listings are a good starting point.

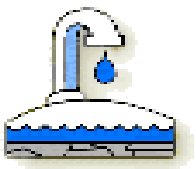
Your local water supplier can give you a list of the chemicals they test for in your water, as well as how your water is treated.

Your state Department of Health/Environment is also a valuable source of information.

For help in locating these agencies or for information on drinking water in general, call: EPAs Safe Drinking Water Hotline: (800) 426-4791.

For additional information on the uses and releases of chemicals in your state, contact the: Community Right-to-Know Hotline: (800) 535-0202.





Revised *January 26, 1998*



Office of Ground Water and Drinking Water

http://www.epa.gov/OGWDW/dwh/c-voc/toluene.html

OPPT Chemical Fact Sheet EPA 749-F-94-021

CHEMICALS IN THE ENVIRONMENT: TOLUENE (CAS NO. 108-88-3)

prepared by
OFFICE OF POLLUTION PREVENTION AND TOXICS
U.S. ENVIRONMENTAL PROTECTION AGENCY
August 1994

Chemicals can be released to the environment as a result of their manufacture, processing, and use. EPA has developed information summaries on selected chemicals to describe how you might be exposed to these chemicals, how exposure to them might affect you and the environment, what happens to them in the environment, who regulates them, and whom to contact for additional information. EPA is committed to reducing environmental releases of chemicals through source reduction and other practices that reduce creation of pollutants.

WHAT IS TOLUENE, HOW IS IT USED, AND HOW MIGHT I BE EXPOSED?

Toluene (also called methyl benzene) is a colorless, flammable liquid. It occurs naturally in petroleum crude oil. Petroleum crude oil is by far the largest source of toluene. Most (up to a billion pounds each year) of this toluene is never isolated from crude oil. Refineries pump this "unrecovered" toluene to some other location where it is added directly to gasoline. The toluene that is isolated is "recovered" in large amounts (approximately 800 million gallons in 1991) by twenty companies in the United States. US demand for toluene is expected to grow moderately over the next several years. The largest users of "recovered" toluene are companies that make benzene. Companies also add toluene to aerosol spray paints, wall paints, lacquers, paint strippers, adhesives, printing ink, spot removers, cosmetics, perfumes, and antifreeze.

Exposure to toluene can occur in the workplace or in the environment following releases to air, water, land, or groundwater. Exposure can also occur when people use gasoline and other products that contain toluene. Toluene enters the body when breathed in with contaminated air or when consumed with contaminated food or water. It can also be absorbed through skin contact. Toluene does not remain in the body due to its breakdown and removal.

WHAT HAPPENS TO TOLUENE IN THE ENVIRONMENT?

Toluene evaporates when exposed to air. It dissolves only slightly when mixed with water. Most direct releases of toluene to the environment are to air. Toluene also evaporates from water and soil exposed to air. Once in air, toluene breaks down to other chemicals. Microorganisms that live in water and in soil can also break down toluene. Because it is a liquid that does not bind well to soil, toluene that makes its way into the ground can move through the ground and enter groundwater. Plants and animals are not likely to store toluene.

HOW DOES TOLUENE AFFECT HUMAN HEALTH AND THE ENVIRONMENT?

Effects of toluene on human health and the environment depend on how much toluene is present and the length and frequency of exposure. Effects also depend on the health of a person or the condition of the environment

when exposure occurs.

Breathing large amounts of toluene for short periods of time adversely affects the human nervous system, the kidneys, the liver, and the heart. Effects range from unsteadiness and tingling in fingers and toes to unconsciousness and death. Direct, prolonged contact with toluene liquid or vapor irritates the skin and the eyes. These effects are not likely to occur at levels of toluene that are normally found in the environment.

Human health effects associated with breathing or otherwise consuming smaller amounts of toluene over long periods of time are not known. Repeatedly breathing large amounts of toluene, such as when "sniffing" glue or paint, can cause permanent brain damage. As a result, humans can develop problems with speech, hearing, and vision. Humans can also experience loss of muscle control, loss of memory, and decreased mental ability. Exposure to toluene can also adversely affect the kidneys. Laboratory animal studies and, in some cases, human exposure studies show that repeat exposure to large amounts of toluene during pregnancy can adversely affect the developing fetus. Other studies show that repeat exposure to large amounts of toluene adversely affects the nervous system, the kidneys, and the liver of animals.

Toluene by itself is not likely to cause environmental harm at levels normally found in the environment. Toluene can contribute to the formation of photochemical smog when it reacts with other volatile organic carbon substances in air.

WHAT EPA PROGRAM OFFICES REGULATE TOLUENE, AND UNDER WHAT LAWS IS IT REGULATED?

EPA OFFICE	LAW	PHONE NUMBER
Pollution Prevention & Toxics	Toxic Substances Control Act	(202) 554-1404
	Emergency Planning and Community Right-to-Know Act (EPCRA) Regulations (Sec. 313)	(800) 535-0202
	Toxics Release Inventory data	(202) 260-1531
Air	Clean Air Act	(919) 541-0888
Solid Waste & Emergency Response	Comprehensive Environmental Response, Compensation, and Liability Act (Superfund)/ Resource Conservation and Recovery Act / EPCRA (Sec. 304/311/312)	(800) 535-0202
Water	Clean Water Act	(202) 260-7588
	Safe Drinking Water Act (Drinking Water Standard: 1.0 mg/L)	(800) 426-4791

A technical support document can be requested from the TSCA Assistance Information Service, (202) 554-1404.

WHAT OTHER FEDERAL AGENCIES OR GROUPS CAN I CONTACT FOR INFORMATION ON TOLUENE?

AGENCY/GROUP	PHONE NUMBER
Agency for Toxic Substances and Disease Registry	(404) 639-6000
American Conference of Governmental Industrial Hygienists	(513) 742-2020
Consumer Product Safety Commission	(301) 504-0994

Food and Drug Administration	(301) 443-3170
National Institute for Environmental Health Sciences (EnviroHealth Clearinghouse)	(800) 643-4794
National Institute for Occupational Safety and Health (NIOSH)	(800) 356-4674
Occupational Safety and Health Administration (Check your local phone book under U.S. Department of Labor)	

EPA 749-F-94-021a

CHEMICAL SUMMARY FOR TOLUENE

prepared by
OFFICE OF POLLUTION PREVENTION AND TOXICS
U.S. ENVIRONMENTAL PROTECTION AGENCY
August 1994

This summary is based on information retrieved from a systematic search limited to secondary sources (see Appendix A). These sources include online databases, unpublished EPA information, government publications, review documents, and standard reference materials. No attempt has been made to verify information in these databases and secondary sources.

I. CHEMICAL IDENTITY AND PHYSICAL/CHEMICAL PROPERTIES

The chemical identity and physical/chemical properties of toluene are summarized in Table 1.

TABLE 1. CHEMICAL IDENTITY AND CHEMICAL/PHYSICAL PROPERTIES OF TOLUENE

Characteristic/Property	Data	Reference
CAS No.	108-88-3	
Common Synonyms	Methyl benzene, Toluol, Phenylmethane	Budavari et al. 1989
Molecular Formula	C7H8	
Chemical Structure		
Physical State	Liquid	Budavari et al. 1989
Molecular Weight	92.13	Budavari et al. 1989
Melting Point	-95øC	Budavari et al. 1989
Boiling Point	110.6øC	Budavari et al. 1989
Water Solubility	470 mg/L @ 16øC; 515 mg/L @ 20øC	Verschueren 1983
Density	0.87 g/mL @ 20øC	Keith and Walters 1985
Vapor Density (air = 1)	3.14	Verschueren 1983
KOC	259	U.S. Air Force 1989
Log KOW	2.73	Leo 1983
Vapor Pressure	22.0 mm Hg @ 20øC	Verschueren 1983
Reactivity	Reacts vigorously with strong oxidizing agents and may generate heat or possibly ignite or explode.	NFPA 1975
Flash Point	4.40øC closed cup	Hawley 1981
Henry's Law Constant	6.61 X 10-3 atm m3/mol @ 25øC	U.S. Air Force 1989
Fish Bioconcentration Factor	20 (in bluegill), 24 (in crayfish)	U.S. EPA 1984
Odor Threshold	2.90 ppm (in air)	U.S. Air Force 1989
Conversion Factors	1 ppm = 3.77 mg/m3 1 mg/m3 = 0.27 ppm	U.S. EPA 1990

II. PRODUCTION, USE, AND TRENDS

A. Production

Almost all toluene is derived from petroleum processing; most is never recovered. This 'contained' toluene, estimated to considerably exceed one billion pounds annually, is incorporated directly into gasoline.

There are 20 toluene-producing companies in the United States with the capacity to isolate at least 15 million gallons per year: Amerada Hess, American Petrofina, Amoco Oil, Ashland Oil, BP Chemicals, Champlin, Chevron Chemical, Coastal Corp., Dow Chemical, Exxon Chemical, Koch Industries, Lyondell Petrochemical, Marathon Oil, Mobil Oil, Oxy Petrochemicals, Phillips Petroleum, Shell Chemical, Sun Company, Texaco, and Triangle Refining. These companies represent over 90 percent of US capacity. Annual production capacity for toluene is estimated at 1.5 to 1.7 billion gallons. In 1991, just over 800 million gallons of toluene were isolated in the US. In the same year, 62 million gallons were imported and 52 million gallons were exported (Mannsville 1992).

B. Use

The largest use for toluene is in the production of benzene. Toluene is also used as an octane booster or enhancer in gasoline, as a raw material for toluene diisocyanate, as a solvent, and in solvent extraction processes. As a solvent, it may be used in aerosol spray paints, wall paints, lacquers, inks, adhesives, natural gums, and resins, as well as in a number of consumer products, such as spot removers, paint strippers, cosmetics, perfumes, and antifreezes. Table 2 shows the estimated 1992 US end-use pattern for toluene.

C. Trends

Demand for toluene in the US is expected to experience modest growth over the next several years. Growth in demand for toluene in gasoline appears to be slowing, and benzene demand is expected to grow at approximately 3 percent per year. Demand for toluene in other uses is expected to remain stable.

TABLE 2. Estimated 1992 United States End-Use Pattern of Toluene

Use of Toluene (typical Standard Industrial Classification (SIC) Code) (see end note 1)	Percentage of all US Toluene Use
Benzene production (production, SIC 2865; use, various industries)	50%
Gasoline blending (production, SIC 2911; sold in SIC 5541; use, various industries)	30%
Toluene diisocyanate production (production, SIC 2865; use, various industries)	7%
Solvents (used in many industries, including 2851 and 2893)	6%
Miscellaneous chemicals (production, SIC 28; use, various industries)	7%

Source: Mannsville 1992.

III. ENVIRONMENTAL FATE

A. Environmental Release

Of the total toluene released to the environment almost all is released to the air. Toluene is a volatile liquid [vapor pressure, 22 mm Hg at 20øC (Verschueren 1983)], and is released into the atmosphere from industrial and consumer uses. The largest sources of toluene release are the evaporation from gasoline, which is 5-7% toluene, and release through car exhausts. Spills of gasoline and industrial releases to surface water and soil are believed to be only a small fraction of the amount released to the atmosphere (ATSDR 1993). In 1992 releases of toluene to environmental media, as reported to the Toxic Chemical Release Inventory by certain types of U.S. industries totaled about 193 million pounds. Of this amount, a total of 191 million pounds (99%) were released to the atmosphere, 84 thousand pounds were released to surface water, 1.6 million pounds were released to underground injection sites, and 708 thousand pounds were released to land (TRI92 1994). Levels of toluene in environmental media range from 1-30 micrograms/m3 in suburban and urban air and 0.1-2.9 micrograms/L in drinking water. Toluene contamination was detected in a maximum of only about 1.2% of the underground water supplies tested, however. The maximum air concentrations of toluene are found indoors and in one study ranged from 37.8 to 71.1 micrograms/m3. The increased concentration compared to urban outside air could originate from household products such as paints, thinners, glue, infiltration from auto emissions, and from cigarette smoke. Cigarettes contain about 80 micrograms toluene/cigarette (ATSDR 1993).

B. Transport

The majority of toluene evaporates to the atmosphere from the water and soil. It is moderately retarded by adsorption to soils rich in organic material (Koc = 259), therefore, transport to ground water is dependent on the soil composition (ATSDR 1993). In unsaturated topsoil containing organic material, it has been estimated that 97% of the toluene is adsorbed to the soil and only about 2% is in the soil-water phase and transported with flowing groundwater. There is little retardation in sandy soils and 2-13% of the toluene was estimated to migrate with flowing water; the remainder was volatilized, biodegraded, or unaccounted for. In saturated deep soils with no soil-air phase, about 48% may be transported with flowing groundwater (U.S. Air Force 1989).

C. Transformation/Persistence

1. Air - The main degradation pathway for toluene in the atmosphere is reaction with photochemically produced hydroxyl radicals. The estimated atmospheric half life for toluene is about 13 hours. Toluene is also oxidized by reactions with atmospheric nitrogen dioxide, oxygen, and ozone, but these are minor degradation pathways. Photolysis is not considered a significant degradative pathway for toluene (ATSDR 1993).

2. Soil - In surface soil, volatilization to air is an important fate process for toluene (U.S. Air Force 1993). Biodegradation of toluene has been demonstrated in the laboratory to occur with

a half life of about 1 hour. In the environment, biodegradation of toluene to carbon dioxide occurs with a typical half life of 1-7 days (ATSDR 1993).

3. Water - An important fate process for toluene is volatilization, the rate of which depends on the amount of turbulence in the surface water (ATSDR 1993). The volatilization of toluene from static water has a half life of 1-16 days, whereas from turbulent water the half life is 5-6 hours. Degradation of toluene in surface water occurs primarily by biodegradation with a half life of less than one day under favorable conditions (presence of microorganisms, microbial adaptation, and optimum temperature). Biodegradation also occurs in shallow groundwater and in salt water at a reduced rate (ATSDR 1993). No data are available on anaerobic degradation of toluene in deep ground water conditions where aerobic degradation would be minimal (ATSDR 1993).

4. Biota - Bioaccumulation in most organisms is limited by the metabolism of toluene into more polar compounds that have greater water solubility and a lower affinity for lipids. Bioaccumulation in the food chain is predicted to be low (ATSDR 1993; U.S. EPA 1990).

IV. HUMAN HEALTH EFFECTS

A. Pharmacokinetics

1. Absorption - Studies in humans and animals have demonstrated that toluene is readily absorbed via the lungs and the gastrointestinal tract. Absorption through the skin is estimated at about 1% of that absorbed by the lungs when exposed to toluene vapor. Dermal absorption is expected to be higher upon exposure to the liquid; however, exposure is limited by the rapid evaporation of toluene (Faust 1994).

2. Distribution - In studies with mice exposed to radiolabeled toluene by inhalation, high levels of radioactivity were present in body fat, bone marrow, spinal nerves, spinal cord, and brain white matter. Lower levels of radioactivity were present in blood, kidney, and liver. Accumulation of toluene has generally been found in adipose tissue, other tissues with high fat content, and in highly vascularized tissues (Faust 1994).

3. Metabolism - The metabolites of inhaled or ingested toluene include benzyl alcohol resulting from the hydroxylation of the methyl group. Further oxidation results in the formation of benzaldehyde and benzoic acid. The latter is conjugated with glycine to yield hippuric acid or reacted with glucuronic acid to form benzoyl glucuronide. o- cresol and p-cresol formed by ring hydroxylation are considered minor metabolites (Faust 1994).

4. Excretion - Toluene is primarily (60-70%) excreted through the urine as hippuric acid. The excretion of benzoyl glucuronide accounts for 10-20%, and excretion of unchanged toluene through the lungs also accounts for 10-20%. Excretion of hippuric acid is usually complete within 24 hours after exposure (U.S. EPA 1990).

B. Acute Toxicity

Humans exposed to intermediate to high levels of toluene for short periods of time experience adverse central nervous system effects ranging from headaches to intoxication, convulsions, narcosis, and death. Similar effects are observed in short-term animal studies.

1. Humans - Toluene ingestion or inhalation can result in severe central nervous system depression, and in large doses, can act as a narcotic. The ingestion of about 60 mL resulted in fatal nervous system depression within 30 minutes in one reported case. Constriction and necrosis of myocardial fibers, markedly swollen liver, congestion and hemorrhage of the lungs and acute tubular necrosis were found on autopsy (Faust 1994).

   Central nervous system effects (headaches, dizziness, intoxication) and eye irritation occurred following inhalation exposure to 100 ppm toluene 6 hours/day for 4 days. Exposure to 600 ppm for 8 hours resulted in the same and more serious symptoms including euphoria, dilated pupils, convulsions, and nausea (U.S. EPA 1994). Exposure to 10,000-30,000 ppm has been reported to cause narcosis and death (U.S. Air Force 1989). Toluene can also strip the skin of lipids causing dermatitis (Keith and Walters 1985).

2. Animals - LD50/LC50 values for rats, reported in the literature searched, are as follows for the various routes of exposure: 5.3-5.9 g/kg (oral), 4618 ppm for 6 hours (respiratory), 1.64 g/kg (i.p. injection) (U.S. EPA 1990). An LC50 value for mice of 5320 ppm for 7 hours was reported, and a rabbit LD50 of 14.1 mL/kg (12.3 g/kg) was reported for dermal exposure (U.S. EPA 1990).

   The initial effects are instability and incoordination, lacrimation and sniffles (respiratory exposure), followed by narcosis. Animals die of respiratory failure from severe nervous system depression. Cloudy swelling of the kidneys was reported in rats following inhalation exposure to 1600 ppm, 18-20 hours/day for 3 days (U.S. EPA 1990).

C. Subchronic/Chronic Effects

Repeat doses of toluene cause adverse central nervous system effects and can damage the upper respiratory system, the liver, and the kidney. Adverse effects occur as a result from both oral and the inhalation exposures. A reported lowest-observed-effect level in humans for adverse neurobehavioral effects is 88 ppm. EPA has derived both an oral RfD (0.2 mg/kg/day) and an inhalation RfC (0.4 mg/m3) for toluene exposures.

1. Humans - Chronic occupational exposure and incidences of toluene abuse have resulted in hepatomegaly and liver function changes. It has also resulted in nephrotoxicity and, in one case, was a cardiac sensitizer and fatal cardiotoxin.

   Neural and cerebellar dystrophy were reported in several cases of habitual "glue sniffing." An epidemiological study in France on workers chronically exposed to toluene fumes reported leukopenia and neutropenia. Exposure levels were not given in the secondary reference; however, the average urinary excretion of hippuric acid, a metabolite of toluene, was given as 4 g/L compared to a normal level of 0.6 g/L (Sandmeyer 1989).

2. Animals - The major target organs for the subchronic/chronic toxicity of toluene are the nervous system, liver, and kidney. Depressed immune response has been reported in male mice given doses of 105 mg/kg/day for 28 days (Faust 1994). Toluene in corn oil administered to F344 male and female rats by gavage 5 days/week for 13 weeks, induced prostration, hypoactivity, ataxia, piloerection, lacrimation, excess salivation, and body tremors at doses ò2500 mg/kg. Liver, kidney, and heart weights were also increased at this dose and histopathologic lesions were seen in the liver, kidneys, brain and urinary bladder. The no-observed-adverse effect level (NOAEL) for the study was 312 mg/kg (223 mg/kg/day) and the lowest-observed-adverse effect level (LOAEL) for the study was 625 mg/kg (446 mg/kg/day) (U.S. EPA 1994). Based on these data, the U.S. EPA (1994) calculated a chronic RfD (reference dose) for toluene of 0.2 mg/kg/day.

   A 13-week gavage study was also performed in B6C3F1 mice. Central nervous system effects were seen including subconvulsive jerking, prostration, impaired grasping reflex, bradypnea, hypothermia, ataxia, and hypoactivity. Body weight loss was seen in males at 2500 mg/kg; however, no other changes were noted. The NOAEL for this study was 1250 mg/kg.

In an inhalation study with toluene, degeneration in the olfactory and respiratory epithelium of the nasal cavity was observed in Fisher 344 rats exposed 6.5 hours/day, 5 days/week for 103 weeks to 600 ppm toluene. A LOAEL of 600 ppm was determined, but a NOAEL could not be determined from the study (U.S. EPA 1994). Based on these data and the LOAEL of 88 ppm (332 mg/m3) from a human epidemiological study (Section IV G), the U.S. EPA (1994) calculated a chronic inhalation reference concentration (RfC) of 0.4 mg/m3 for toluene from the human exposure data.

D. Carcinogenicity

There is inadequate evidence for the carcinogenicity of toluene in both human and animal studies.

1. Humans - Epidemiology studies revealed no significant increased risk for cancer among workers who were exposed to toluene for at least 5 years. In one study, the incidence of respiratory tract tumors was increased among all workers exposed for a minimum of 3 months. However, when only those workers exposed for 5 years and a latency period of 10 years were considered, the significance of the increase was lost. In another study, the cohort exposed to toluene and other chemicals experienced fewer cancer deaths than the general population (Faust 1994).

2. Animals - Sprague-Dawley rats were given 500 mg toluene/kg 4-5 days/week for 2 years. At the end of the study, 8% of the treated males and 17.5% of the treated females developed hemolymphoreticular neoplasms compared to 7% of the male and 3% of the female controls. Two long-term inhalation studies in rats and mice found no evidence of toluene carcinogenicity. Rats were given up to 300 ppm, 6 hours/day, 5 days/week for 24 months. Mice were given 600 or 1200 ppm, 6.5 hours/day, 5 days/week for 24 months.

   Based on no human and inadequate animal data, the U.S. EPA

cancer classification for toluene is D, not classified (U.S. EPA 1994).

E. Genotoxicity

Toluene has been extensively tested in a variety of genotoxicity tests. Toluene has been shown to be negative for gene mutations in bacteria, in yeast, and in the fruit fly.

Conflicting results have been reported in mammalian cell tests. In vitro mammalian cell tests (including human cells) for sister chromatid exchange and chromosome aberrations have been reported as negative. Toluene was positive in rodent micronucleus tests when administered by injection but negative when administered by the oral route (McGregor 1994).

F. Developmental/Reproductive Toxicity

Exposures to high levels of toluene can result in adverse effects in the developing human fetus. Several studies have indicated that high levels of toluene can also adversely effect the developing offspring in laboratory animals.

1. Humans - Variable growth, microcephaly, CNS dysfunction, attentional deficits, minor craniofacial and limb abnormalities, and developmental delay were seen in three children exposed to toluene in utero as a result of maternal solvent abuse before and during pregnancy (U.S. EPA 1994).

2. Animals - Sternebral alterations, extra ribs, and missing tails were reported following treatment of CFY rats with 1500 mg/m3 toluene 24 hours/day during days 9-14 of gestation. Two of the dams died during the exposure.

   Another group of CFY rats received 1000 mg/m3 8 hours/day during days 1-21 of gestation. No maternal deaths or toxicity occurred, however, minor skeletal retardation was present in the exposed fetuses. CFLP Mice were exposed to 500 or 1500 mg/m3 toluene continuously during days 6-13 of pregnancy. All dams died at the high dose during the first 24 hours of exposure, however none died at 500 mg/m3. Decreased fetal weight was reported, but there were no differences in the incidences of skeletal malformations or anomalies between the treated and control offspring (U.S. EPA 1994).

G. Neurotoxicity

Available information indicate that toluene adversely affects the central nervous system of humans (by inhalation) and of laboratory animals (by oral and inhalation).

1. Humans - A battery of neurobehavioral tests were administered to workers exposed to 88 ppm (332 mg/m3, TWA) toluene and to a control group exposed to 13 ppm (49 mg/m3). A lowest-observed-adverse effect level (LOAEL) of 88 ppm (332 mg/m3) for neurobehavioral changes was determined (U.S.EPA 1994). Nervous system effects including fatigue, muscular weakness, confusion, impaired coordination, slight exhilaration, enlarged pupils and accommodation disturbances were reported in humans chronically exposed to 200-800 ppm toluene, 7-8 hours/day (U.S. EPA 1994). Exposure to 100 ppm for 6 hours

resulted in fatigue, sleepiness, decreased manual dexterity, decreased color discrimination, and decreased accuracy in visual perception. The concentration of 100 ppm is roughly equivalent to 40.39 mg/kg over the 6-hour period.

Prolonged abuse was reported to result in altered electroencephalogram, ataxia, tremors, CNS atrophy, and impaired speech, hearing, and vision (ATSDR 1993).

Magnetic resonance imaging and brainstem auditory evoked response evaluations of the brains of chronic solvent abusers indicate that there are permanent changes in brain structure that correlate with the degree of dysfunction suggesting the neurological symptoms may result from permanent structural changes in the brain (ATSDR 1993).

2. Animals - Alterations in the concentrations of CNS neurotransmitters were reported in male CD-1 mice following treatment with 5-105 mg toluene/kg/day given in drinking water for 28 days. The neurotransmitters affect mood, emotional state, and aggressive behavior. Exposure of mice to 1250 and 2500 mg/kg/day for 13 weeks resulted in increased relative brain weight in male mice at 2500 mg/kg/day and necrosis of brain tissue at both doses. Acute inhalation exposure of monkeys to 1000 and 2000 ppm toluene, which are below the concentrations known to cause neurological impairment, were reported to impair cognitive and motor abilities. Disturbances in the vestibular and optooculomotor systems of rats resulted from acute exposure to 1500 ppm toluene. Exposure of rats to 1500 ppm for 1 hour/day for 14 days also resulted in nystagmus. The cerebellum was suggested as a target site of toluene (ATSDR 1993). Exposure of rats to 1200 ppm for 5 weeks or 1000 ppm for 2 weeks produced permanent high-frequency hearing loss. The hearing loss occurred whether or not the exposure was continuous or episodic and was compounded by post-exposure high noise levels (ATSDR 1993). Decreased neuromuscular performance has been recorded in several studies. A single exposure for 4 hours to 810-6250 ppm toluene resulted in impaired performance in tests designed to measure neuromuscular performance. Daily 15 minute exposure to toluene for up to 4 weeks resulted in a dose-related increase on righting-reflex latency time. A decline in the ability of animals to perform trained neuromuscular responses was also seen following exposure of rats to 125-500 ppm toluene for 4 hours. In this case, recovery occurred in about 2 hours (ATSDR 1993).

V. ENVIRONMENTAL EFFECTS

A. Toxicity to Aquatic Organisms

Toluene has moderate acute toxicity to aquatic organisms; several toxicity values are in the range of greater than 1 mg/L and 100 mg/L. Ninety-six-hour LC50 values for fish are: 12.6-72.0 mg/L for Pimephales promelas (fathead minnow), 13-24 mg/L for Lepomis macrochirus (bluegill), 28.2-59.3 mg/L for Poecilia reticulata (guppy), 240 mg/L for Ictalurus punctatus (channel catfish), and 22.8-57.68 g/L for Carassius auratus (goldfish) (AQUIRE 1994). Ninety-six-hour LC50 values for crustaceans are: 9.5 ppm for Palaemonetes pugio (grass shrimp), 28 ppm for Cancer magister (crab larvae stage 1), 4.3 ppm for Crangon franciscorum (shrimp),

and 9.5 mg/L for Palaemonetes pugio (daggerblade grass shrimp) (AQUIRE 1994). The EC50 values for various parameters in algae are: 245 mg/L, growth, 24 hours for Chlorella vulgaris (green algae); 20 mg/L, photosynthesis effect, 8 hours for Skeletonema costatum (diatom); and 12.5 mg/L, growth, 72 hours for Selenastrum capricornutum (green algae) (AQUIRE 1994).

B. Toxicity to Terrestrial Organisms

No information was found in the secondary sources searched for terrestrial organism toxicity. The oral LD50 in the rat, 5.3-5.9 g/kg), suggests that the chemical would not be acutely toxic to terrestrial animals unless present in very high concentrations. Studies in laboratory animals also suggest that toluene would not cause developmental/reproductive effects in terrestrial species at expected environmental levels (see section IV.F).

C. Abiotic Effects

No information on abiotic effects of toluene was located in the secondary references. According to the definition provided in the Federal Register (1992), toluene is a volatile organic compound (VOC) substance. As a VOC, toluene can contribute to the formation of photochemical smog in the presence of other VOCs.

VI. EPA/OTHER FEDERAL/OTHER GROUP ACTIVITY

Voluntary reduction of toluene environmental releases has occurred since 1991, as a result of a joint industry/EPA pollution prevention initiative, the 33/50 program. The Clean Air Act Amendments of 1990 list toluene as a hazardous air pollutant. Occupational exposure to toluene is regulated by the Occupational Safety and Health Administration (OSHA). The permissible exposure limit (PEL) is 200 parts per million parts of air (ppm) as an 8-hour time-weighted average (TWA) (29 CFR 1910.1000).

Federal agencies and other groups that can provide additional information on toluene are listed in Tables 3 and 4.

TABLE 3. EPA OFFICES AND CONTACT NUMBERS FOR INFORMATION ON TOLUENE

EPA OFFICE	LAW	PHONE NUMBER
Pollution Prevention & Toxics	Toxic Substances Control Act (Sec. 8A/8D/8E)	(202) 554-1404
	Emergency Planning and Community Right-to-Know Act (EPCRA)	
	Regulations (Sec. 313)	(800) 535-0202
	Toxics Release Inventory data	(202) 260-1531
Air	Clean Air Act	(919) 541-0888
Solid Waste & Emergency Response	Comprehensive Environmental Response, Compensation, and Liability Act (Superfund)/ Resource Conservation and Recovery Act / EPCRA (Sec. 304/311/312)	(800) 535-0202
Water	Clean Water Act	(202) 260-7588
	Safe Drinking Water Act (Drinking Water Standard: 1.0 mg/L)	(800) 426-4791

TABLE 4. OTHER FEDERAL OFFICES/OTHER GROUP CONTACT NUMBERS FOR INFORMATION ON TOLUENE

Other Agency/Department/Other Group	Contact Number
Agency of Toxic Substances & Disease Registry	(404) 639-6000
American Conference of Governmental Industrial Hygienists (Recommended Exposure Limit: 50 ppm)	(513) 742-2020
Consumer Product Safety Commission	(301) 504-0994
Food & Drug Administration	(301) 443-3170
National Institute for Environmental Health Sciences (EnviroHealth Clearinghouse)	(800) 643-4794
National Institute for Occupational Safety & Health (Recommended Exposure Limit: 100 ppm)	(800) 356-4674
Occupational Safety & Health Administration (Permissible Exposure Limit: 200 ppm)	Check local phone book for phone number under Department of Labor

VII. END NOTES

1. Standard Industrial Classification code is the statistical classification standard for all Federal economic statistics. The code provides a convenient way to reference economic data on industries of interest to the researcher. SIC codes presented here are not intended to be an exhaustive listing; rather, the codes listed should provide an indication of where a chemical may be most likely to be found in commerce.

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APPENDIX A. SOURCES SEARCHED FOR FACT SHEET PREPARATION

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International Chemical Safety Cards

TOLUENE

ICSC: 0078

TOLUENE
Methylbenzene
Toluol
$C_6H_5CH_3/C_7H_8$
Molecular mass: 92.1

CAS # 108-88-3
RTECS # XS5250000
ICSC # 0078
UN # 1294
EC # 601-021-00-3



TYPES OF HAZARD/ EXPOSURE	ACUTE HAZARDS/ SYMPTOMS	PREVENTION	FIRST AID/ FIRE FIGHTING
FIRE	Highly flammable.	NO open flames, NO sparks, and NO smoking.	Powder, AFFF, foam, carbon dioxide.
EXPLOSION	Vapour/air mixtures are explosive.	Closed system, ventilation, explosion-proof electrical equipment and lighting. Prevent build-up of electrostatic charges (e.g., by grounding). Do NOT use compressed air for filling, discharging, or handling.	In case of fire: keep drums, etc., cool by spraying with water.
EXPOSURE		STRICT HYGIENE! AVOID EXPOSURE OF (PREGNANT) WOMEN!	
• **INHALATION**	Dizziness. Drowsiness. Headache. Nausea. Unconsciousness.	Ventilation, local exhaust, or breathing protection.	Fresh air, rest. Artificial respiration if indicated. Refer for medical attention.
• **SKIN**	Dry skin. Redness.	Protective gloves.	Remove contaminated clothes. Rinse and then wash skin with water and soap. Refer for medical attention.

• **EYES**	Redness. Pain.	Safety goggles or face shield.	First rinse with plenty of water for several minutes (remove contact lenses if easily possible), then take to a doctor.
• **INGESTION**	Abdominal pain. Burning sensation (further see Inhalation).	Do not eat, drink, or smoke during work.	Rinse mouth. Give a slurry of activated charcoal in water to drink. Do NOT induce vomiting. Refer for medical attention.

SPILLAGE DISPOSAL	STORAGE	PACKAGING & LABELLING
Collect leaking liquid in sealable containers. Absorb remaining liquid in sand or inert absorbent and remove to safe place. Do NOT wash away into sewer (extra personal protection: self-contained breathing apparatus).	Fireproof. Separated from strong oxidants.	F symbol Xn symbol R: 11-20 S: (2-)16-25-29-33 UN Hazard Class: 3 UN Packing Group: II

SEE IMPORTANT INFORMATION ON BACK

ICSC: 0078

Prepared in the context of cooperation between the International Programme on Chemical Safety & the Commission of the European Communities © IPCS CEC 1993 No modifications to the International version have been made except to add the OSHA PELs, NIOSH RELs and IDLH values.

International Chemical Safety Cards

TOLUENE

ICSC: 0078

IMPORTANT

PHYSICAL STATE; APPEARANCE:
COLOURLESS LIQUID , WITH CHARACTERISTIC ODOUR.

PHYSICAL DANGERS:
The vapour is heavier than air and may travel along the ground; distant ignition possible. As a result of flow, agitation, etc., electrostatic charges can be generated.

CHEMICAL DANGERS:
Reacts violently with strong oxidants causing fire and explosion hazard.

OCCUPATIONAL EXPOSURE LIMITS (OELs):
TLV: 50 ppm; 188 mg/m^3 (as TWA) (skin) (ACGIH 1993-1994).
OSHA PEL: TWA 200 ppm C 300 ppm 500 ppm (10-minute maximum peak)
NIOSH REL: TWA 100 ppm (375 mg/m^3) ST

ROUTES OF EXPOSURE:
The substance can be absorbed into the body by inhalation, through the skin and by ingestion.

INHALATION RISK:
A harmful contamination of the air can be reached rather quickly on evaporation of this substance at 20°C.

EFFECTS OF SHORT-TERM EXPOSURE:
The substance irritates the eyes and the respiratory tract. Exposure could cause central nervous system depression. Exposure at high levels may result in cardiac dysrhythmia, unconsciousness and death.

EFFECTS OF LONG-TERM OR REPEATED EXPOSURE:
Repeated or prolonged contact with skin may

D A T A	150 ppm (560 mg/m^3) NIOSH IDLH: 500 ppm	cause dermatitis. The substance may have effects on the central nervous system , resulting in decreased learning ability and psychological disorders. Animal tests show that this substance possibly causes toxic effects upon human reproduction.
PHYSICAL PROPERTIES	Boiling point: 111°C Melting point: -95°C Relative density (water = 1): 0.87 Solubility in water: none Vapour pressure, kPa at 20°C: 2.9 Relative vapour density (air = 1): 3.2	Relative density of the vapour/air-mixture at 20°C (air = 1): 1.06 Flash point: 4°C c.c.°C Auto-ignition temperature: 480°C Explosive limits, vol% in air: 1.1-7.1 Octanol/water partition coefficient as log Pow: 2.69
ENVIRONMENTAL DATA		

N O T E S

Depending on the degree of exposure, periodic medical examination is indicated.

Transport Emergency Card: TEC (R)-31
NFPA Code: H 2; F 3; R 0;

ADDITIONAL INFORMATION

ICSC: 0078 **TOLUENE**

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IMPORTANT LEGAL NOTICE:	Neither NIOSH, the CEC or the IPCS nor any person acting on behalf of NIOSH, the CEC or the IPCS is responsible for the use which might be made of this information. This card contains the collective views of the IPCS Peer Review Committee and may not reflect in all cases all the detailed requirements included in national legislation on the subject. The user should verify compliance of the cards with the relevant legislation in the country of use. The only modifications made to produce the U.S. version is inclusion of the OSHA PELs, NIOSH RELs and IDLH values.

Level 1

Chemical Name: Toluene

CAS Registry Number: 108-88-3

Click on red circle(s) to obtain data.

Risk Value	ATSDR	Health Canada	ITER	RIVM	U.S.EPA	WHO/IPCS
Noncancer Oral	●	●	●	●	●	●
Cancer Oral	●	●	●	●	●	●
Noncancer Inhalation	●	●	●	●	●	●
Cancer Inhalation	●	●	●	●	●	●

Glossary of ITER definitions

ITER Instructions

WHAT'S NEW | SUPPORT ITER | ITER HOME | RETURN

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CTC Concurrent Technologies Corporation

Toxicology Excellence for Risk Assessment

TERA

NTP CHEMICAL REPOSITORY (RADIAN CORPORATION, AUGUST 29, 1991)
TOLUENE

-IDENTIFIERS
 ===========

*CATALOG ID NUMBER: 000104

*CAS NUMBER: 108-88-3

*BASE CHEMICAL NAME: TOLUENE

*PRIMARY NAME: TOLUENE

*CHEMICAL FORMULA: C7H8

*STRUCTURAL FORMULA: C6H5CH3

*WLN: 1R

*SYNONYMS:
  METHYLBENZENE
  METHACIDE
  PHENYLMETHANE
  METHYLBENZOL
  TOLUOL
  TOLU-SOL
  RCRA WASTE NUMBER U220
  UN 1294
  ANTISAL 1A
  NCI-C07272
  BENZENE, METHYL-
  METHANE, PHENYL-

-PHYSICAL CHEMICAL DATA
 ======================

*PHYSICAL DESCRIPTION: LITERATURE: Clear, colorless to amber liquid
                       REPOSITORY: Clear colorless liquid

*MOLECULAR WEIGHT: 92.14

*SPECIFIC GRAVITY: 0.8669 @ 20/4 C [017,047,430]

*DENSITY: 0.867 g/mL [269,275]

*MP (DEG C): -95 C [205,371,421,430]

*BP (DEG C): 110.6 C [025,051,205,371]

*SOLUBILITIES:
       WATER : <1 mg/mL @ 18 C (RAD)

        DMSO : >=100 mg/mL @ 18 C (RAD)

 95% ETHANOL : >=100 mg/mL @ 18 C (RAD)

    METHANOL : Not available

ACETONE : >=100 mg/mL @ 18 C (RAD)

TOLUENE : Not available

OTHER SOLVENTS:
Alcohol: Soluble [017,053,062,430]
Organic solvents: Miscible [295,421]
Ligroin: Soluble [017]
Chloroform: Miscible [033,043,051,205]
Glacial acetic acid: Miscible [033,051,295]
Carbon disulfide: Miscible [033,051]
Ether: Miscible [033,043,051,205]
Benzene: Soluble [017,053,062]

*VOLATILITY:
Vapor pressure: 10 mm Hg @ 6.4 C, 20 mm Hg @ 18.4 C, 40 mm Hg @ 31.8 C [038]
Vapor density : 3.14 [043,051,071,102]

*FLAMMABILITY(FLASH POINT):
This chemical has a flash point of 4.4 C (40 F) [033,043,421,430]. It is flammable. Fires involving this material can be controlled with a dry chemical, carbon dioxide or Halon extinguisher. A water spray may also be used [051,071]. Vapor trail flash-back can occur [371,451]. The autoignition temperature for this compound is 536 C (997 F) [036,062,371].

*UEL: 7.1% [051,058,421,451] LEL: 1.27% [043,058,102,371]

*REACTIVITY:
This compound reacts violently with 1,3-dichloro-5,5-dimethyl-2,4-imidazolididione, dinitrogen tetraoxide, concentrated nitric acid, (H_2SO_4 + NO_3), $AgClO_4$, BrF_3, UF_6, tetranitromethane and oxidizing materials [043]. It is incompatible with oxygen [058]. It may attack some forms of plastics, rubber and coatings [102].

*STABILITY:
This compound is hygroscopic [269]. Solutions of this chemical in water, DMSO, 95% ethanol or acetone should be stable for 24 hours under normal lab conditions (RAD).

*OTHER PHYSICAL DATA:
Refractive index: 1.4968 @ 20 C [269,275]
Boiling point: 14.5 C @ 14.5 mm Hg [017]
Benzene-like odor [033,062,346,430]
Critical temperature: 318.6 C [371]
Critical pressure: 30400 mm Hg [371]
Floats on water [051,071,371,451]
Dissolves slowly in water [051,071,371]
100% Volatile by volume [058]
Evaporation rate (butyl acetate = 1): >1 [058]
Vapors are heavier than air [058,371]
Burns with a smoky flame [295]
Odor threshold: 0.17 ppm [371]
Burning rate: 5.7 mm/min [371]
Liquid surface tension: 29 dynes/cm @ 20 C [371]
log P octanol: 2.69 @ 20 C [055]
Liquid water interfacial tension: 36.1 dynes/cm [371]
Latent heat of vaporization: 86.1 cal/g [371]
Heat of combustion: -9686 cal/g [371]
Heat of fusion: 17.17 cal/g [371]
Lambda max (in methanol): 269 nm, 265 nm (shoulder), 262 nm, 260 nm (shoulder), 256 nm, 254 nm (shoulder), 249 nm (shoulder), 243 nm (shoulder),

238 nm (shoulder) (epsilon = 227.1, 169.5, 254.6, 212.6, 190.2, 178.2, 125.6, 72.63, 38.8) [052]

-TOXICITY
========

*NIOSH REGISTRY NUMBER: XS5250000

*TOXICITY:

typ. dose	mode	specie	amount	units	other
TCLo	ihl	hmn	200	ppm	
TCLo	ihl	man	100	ppm	
LD50	orl	rat	5000	mg/kg	
LCLo	ihl	rat	4000	ppm/4H	
LD50	ipr	rat	1332	mg/kg	
LD50	unr	rat	6900	mg/kg	
LC50	ihl	mus	5320	ppm/8H	
LD50	ipr	mus	640	mg/kg	
LD50	unr	mus	2000	mg/kg	
LD50	skn	rbt	12124	mg/kg	
LCLo	ihl	gpg	1600	ppm	
LDLo	scu	frg	920	mg/kg	
LDLo	orl	hmn	50	mg/kg	
LD50	ivn	rat	1960	mg/kg	
LD50	scu	mus	2250	mg/kg	
LDLo	ivn	rbt	130	mg/kg	
LCLo	ihl	rbt	55000	ppm/40M	
LDLo	ipr	gpg	4681	mg/kg	
LDLo	ipr	mam	1750	mg/kg	

*AQTX/TLM96: Not available

*SAX TOXICITY EVALUATION:
THR: Poison by intraperitoneal route. Moderately toxic by intravenous, subcutaneous and possibly other routes. Mildly toxic by inhalation. An experimental teratogen. Human systemic effects by inhalation. Experimental reproductive effects. Mutagenic data. A human eye irritant. An experimental skin and severe eye irritant. In the few cases of acute poisoning reported, the effect has been that of a narcotic, the workman passing through a stage of intoxication into one of coma. Recovery following removal from exposure has been the rule. A common air contaminant.

*CARCINOGENICITY:
Review: IARC Cancer Review: Human Inadequate Evidence
IARC Cancer Review: Animal Inadequate Evidence
IARC: Not classifiable as a human carcinogen (Group 3) [610]
Status: NTP Carcinogenesis Studies (Inhalation); No Evidence: Male and Female Rat, Male and Female Mouse [620]

*MUTATION DATA: See RTECS printout for data

*TERATOGENICITY: See RTECS printout for data

*STANDARDS, REGULATIONS & RECOMMENDATIONS:
OSHA: Federal Register (1/19/89) and 29 CFR 1910.1000 Subpart Z
Transitional Limit: PEL-TWA 200 ppm; Ceiling Limit 300 ppm; Peak 500 ppm/10M [015,327,545,610]
Final Limit: PEL-TWA 100 ppm; STEL 150 ppm [015,545,610]
ACGIH: TLV-TWA 100 ppm; STEL 150 ppm [015,415,421,610]

NIOSH Criteria Document: Recommended Exposure Limit to this compound-air:
TWA 100 ppm; Ceiling Limit 200 ppm/10M [015,610]
NFPA Hazard Rating: Health (H): 2
Flammability (F): 3
Reactivity (R): 0
H2: Materials hazardous to health, but areas may be entered freely with full-faced mask self-contained breathing apparatus which provides eye protection (see NFPA for details).
F3: Materials which can be ignited under almost all normal temperature conditions (see NFPA for details).
R0: Materials which are normally stable even under fire exposure conditions and which are not reactive with water (see NFPA for details).

*OTHER TOXICITY DATA:
Skin and Eye Irritation Data:

eye-hmn	300 ppm
skn-rbt	435 mg MLD
skn-rbt	20 mg/24H MOD
skn-rbt	500 mg MOD
eye-rbt	870 ug MLD
eye-rbt	2 mg/24H SEV
eye-rbt	100 mg/30S rns MLD

Review: Toxicology Review-7
Standards and Regulations: DOT-Hazard: Flammable liquid; Label: Flammable liquid
Status: EPA Genetox Program 1988, Negative: Cell transform.-SA7/SHE; In vitro SCE-human
EPA Genetox Program 1988, Negative: Sperm morphology-mouse
EPA Genetox Program 1988, Inconclusive: E coli polA without S9
EPA TSCA Chemical Inventory, 1986
EPA TSCA Test Submission (TSCATS) Data Base, January 1990
NIOSH Analytical Methods: see Hydrocarbons, Aromatic, 1501; Hydrocarbons, BP 36-126 C, 1500
NIOSH Analytical Methods: see Toluene, 4000; 2-Butanone, Ethanol, and Toluene in blood, 8002
EPA TSCA 8(a) Preliminary Assessment Information, Final Rule
EPA TSCA Section 8(e) Status Report 8EHQ-0680-0345
EPA TSCA Section 8(e) Status Report 8EHQ-1080-0368
EPA TSCA Section 8(e) Status Report 8EHQ-0278-0079 P
IDLH value: 2000 ppm [071,371]

-OTHER DATA (Regulatory)
==========

*PROPER SHIPPING NAME (IATA): Toluene

*UN/ID NUMBER: UN1294

*HAZARD CLASS: 3 SUBSIDIARY RISK: None PACKING GROUP: II

*LABELS REQUIRED: Flammable liquid

*PACKAGING: PASSENGER: PKG. INSTR.: 305, Y305 MAXIMUM QUANTITY: 5 L, 1 L
CARGO : PKG. INSTR.: 307 MAXIMUM QUANTITY: 60 L

*SPECIAL PROVISIONS: None

*USES:
This compound is used to manufacture benzoic acid, benzaldehyde, benzene, phenol, caprolactam, linoleum, toluenediisocyanates (polyurethane resins),

toluene sulfonates (detergents), artificial leather and fabric and paper coatings. It is also used in explosives, dyes and other organic compounds, as a solvent for paints, lacquers, gums, most oils, rubber, vinyl organosols and resins, in the extraction of various principles of plants, as a gasoline additive, as a diluent and thinner in nitrocellulose lacquers, as an adhesive solvent in plastic toys and model airplanes, in saccharin, perfumes and scintillation counters, in photogravure color-printing process, in the cleaning industry, in the impregnation of cartridge paper, as a solvent in pharmaceutical and plastic industries, as an insecticide, as a urine preservative for chemical examination and as an asphalt and naphtha constituent.

*COMMENTS:
This compound is obtained from coal tar and petroleum [055,421].

-HANDLING PROCEDURES
==========

*ACUTE/CHRONIC HAZARDS:
This compound may cause irritation of the respiratory tract, mucous membranes and throat [051]. It may also cause eye and skin irritation [053, 058,102,346]. It may be harmful by inhalation, ingestion or skin absorption [036,051,071,269]. It is readily absorbed through the skin [269]. When heated to decomposition it emits toxic fumes of carbon dioxide and carbon monoxide [102,269].

*MINIMUM PROTECTIVE CLOTHING: Not available

*RECOMMENDED GLOVE MATERIALS:
GlovES+ Expert System Glove Types For The Neat (Undiluted) Chemical:
This chemical has not been tested for permeation by Radian Corporation; however, the GlovES+ expert system was used to extrapolate permeation test information from compounds in the same chemical class. The GlovES+ system uses permeation data from literature sources; therefore, extra safety margins should be used with the estimated protection time(s). If this chemical makes direct contact with your glove, or if a tear, puncture or hole develops, replace them at once.
The GlovES+ expert system is a tool that can help people better manage protection from chemicals, however this tool cannot replace sound judgment nor make technical decisions. Our GlovES+ expert system is designed to offer initial advice and assistance in glove selection while the final glove selection should be made by knowledgeable individuals based on the specific circumstances involved.

Glove Type	Model Number	Thickness	Estimated Protection Time
PE/EVAL/PE	Safety 4 4H	0.07 mm	240 min
PVA	Edmont 25-545	unknown	360 min
Unknown	North Silvershield	0.08 mm	360 min
Viton	North F-091	0.24 mm	480 min

Permeation Test Results of Diluted Chemical in corn oil (50%):
The permeation test results for solutions of this chemical are given below. The breakthrough times of the diluted chemicals at the given concentration are given for each glove type tested. The table is a presentation of actual test results, not specific recommendations or suggestions. Avoid glove types which exhibit breakthrough times of less than the anticipated task time plus an adequate safety factor. If this chemical makes direct contact with your glove, or if a tear, puncture or hole develops, replace them at once.

Glove Type	Model Number	Thickness	Breakthrough Time

Nitrile	Edmont 37-175	0.64 mm	98 min
Butyl Rubber	North B-174	0.38 mm	46 min
PVA	Edmont 29-250	0.46 mm	6 min

*RECOMMENDED RESPIRATOR:
Where the neat test chemical is weighed and diluted, wear a NIOSH-approved half face respirator equipped with an organic vapor/acid gas cartridge (specific for organic vapors, HCl, acid gas and SO2) with a dust/mist filter.

*OTHER: Not available

*STORAGE PRECAUTIONS:
You should store this chemical in an explosion-proof refrigerator and keep it away from moisture. If possible, it would be prudent to store this compound under inert atmosphere. STORE AWAY FROM SOURCES OF IGNITION.

*SPILLS AND LEAKAGE:
If you spill this chemical, FIRST REMOVE ALL SOURCES OF IGNITION. Then, use absorbent paper to pick up all liquid spill material. Your contaminated clothing and absorbent paper should be sealed in a vapor-tight plastic bag for eventual disposal. Solvent wash all contaminated surfaces with 60-70% ethanol followed by washing with a soap and water solution. Do not reenter the contaminated area until the Safety Officer (or other responsible person) has verified that the area has been properly cleaned.

*DISPOSAL AND WASTE TREATMENT: Not available

-EMERGENCY PROCEDURES
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*SKIN CONTACT:
IMMEDIATELY flood affected skin with water while removing and isolating all contaminated clothing. Gently wash all affected skin areas thoroughly with soap and water.
If symptoms such as redness or irritation develop, IMMEDIATELY call a physician and be prepared to transport the victim to a hospital for treatment.

*INHALATION:
IMMEDIATELY leave the contaminated area; take deep breaths of fresh air. If symptoms (such as wheezing, coughing, shortness of breath, or burning in the mouth, throat, or chest) develop, call a physician and be prepared to transport the victim to a hospital.
Provide proper respiratory protection to rescuers entering an unknown atmosphere. Whenever possible, Self-Contained Breathing Apparatus (SCBA) should be used; if not available, use a level of protection greater than or equal to that advised under Respirator Recommendation.

*EYE CONTACT:
First check the victim for contact lenses and remove if present. Flush victim's eyes with water or normal saline solution for 20 to 30 minutes while simultaneously calling a hospital or poison control center.
Do not put any ointments, oils, or medication in the victim's eyes without specific instructions from a physician.
IMMEDIATELY transport the victim after flushing eyes to a hospital even if no symptoms (such as redness or irritation) develop.

*INGESTION:
DO NOT INDUCE VOMITING. If the victim is conscious and not convulsing, give 1 or 2 glasses of water to dilute the chemical and IMMEDIATELY call a

hospital or poison control center. Be prepared to transport the victim to a hospital if advised by a physician.

If the victim is convulsing or unconscious, do not give anything by mouth, ensure that the victim's airway is open and lay the victim on his/her side with the head lower than the body. DO NOT INDUCE VOMITING. IMMEDIATELY transport the victim to a hospital.

*SYMPTOMS:

Symptoms of exposure to this compound include eye irritation, dilation of the pupils, impairment of reaction in association with fatigue, slight pallor of the fundi, inebriation, ocular disturbances and reddening of vision [099]. It may cause dizziness, headache, nausea, mental confusion, blood disease and dermatitis [036]. It may also cause giddiness [071]. Other symptoms may include hallucinations or distorted perceptions, narcosis in high concentrations, motor activity changes. An occasional report of chronic poisoning describes an anemia and leucopenia. It causes loss of appetite, a bad taste, lassitude, impairment of coordination and reaction time and an enlarged liver [043]. It may cause central nervous system depression, bone marrow depression, petechial hemorrhages, noncoagulated blood, congestion of all organs, severe bone marrow aplasia, necrosis or fatty degeneration of the heart, liver and adrenals, weakness, euphoria, vomiting, tightness in the chest, blurred vision, tremors, shallow and rapid respiration, ventricular irregularities including fibrillation, paralysis, convulsions, violent excitement or delirium, unconsciousnes, kidney or liver damage, skin irritation, scaling and cracking, drowsiness, nervousness, pallor, petechiae, abnormal bleeding, irreversible encephalopathy with ataxia, tremulousness, emotional lability, diffuse cerebral atrophy and death [301]. It may also cause abnormal tendon reflexes, reduced grasping power, decreased finger agility, metabolic acidosis, hepatomegaly, exhilaration, lightheadedness, cardiovascular collapse, cardiac arrhythmias, bradycardia, mydrasis, insomnia, restlessness, staggering gait, lack of self-control, stupor, increased irritability (personality changes), exaggerated mood swings, equilibrium disorders and vertigo [051]. Symptoms of exposure may include skin sensation such as a pins and needles feeling or numbness and difficulty in seeing bright light [102]. It may cause high urinary pH, nightmares, vertical nystagmus and status epilepticus [295]. It may also cause loss of memory, anorexia, palpitation and aplastic anemia [421]. Other symptoms include renal but also neural and especially cerebellar dystrophy, lacrimation, hilarity, nasal mucous secretion and metallic taste. High concentrations may result in paresthesia, collapse, cardiac sensitization and fatal cardiotoxicity [430]. It may cause irritation to the nose and throat, respiratory arrest, coughing, gagging, distress, pulmonary edema, griping and diarrhea [371]. It may also cause chemical pneumonitis, coma and conjunctivitis [058].

-SOURCES
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Web Sites

that offer searchable chemical databases, recommended by Scorecard

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If you want more detailed information about a chemical than Scorecard provides, there are several on-line and library resources Scorecard recommends for further research.

ON-LINE CHEMICAL DATABASES

CambridgeSoft Chemfinder
http://chemfinder.camsoft.com/

Search

Chemfinder gives basic physico-chemical data and molecular structures for chemicals, and provides links to international data sources addressing specific chemicals.

Hazardous Substances Data Bank
http://toxnet.nlm.nih.gov/

Search

HSDB focuses on the toxicology of potentially hazardous chemicals, and includes peer-reviewed information on human exposure, industrial hygiene, emergency handling procedures, environmental fate, and regulatory requirements.

University of Akron Hazardous Chemicals Database
http://ull.chemistry.uakron.edu/erd/

Search

The Hazardous Chemicals Database provides physical data on chemicals and links to Department of Transportation safety guides that are valuable for emergency response.

BIBLIOGRAPHIC RESOURCES ON CHEMICAL TOXICITY

Scorecard provides qualitative summaries of the health hazards posed by a chemical (e.g., it is a suspected neurotoxicant), but not direct access to supporting toxicological data. These scientific studies are abstracted in several toxicity databases, which are available in libraries, from commercial vendors, and sometimes on-line. The major toxicity databases include:

The Registry of Toxic Effects of Chemicals Substances (RTECS)
RTECS is a database of toxicological information compiled by the National Institute for Occupational Safety and Health. It contains summary information about the types of health effects chemicals can cause and the concentrations at which toxicity is known to occur. It is available from several commercial vendors at http://www.cdc.gov/niosh/rtecs.html, and can often be found at major public or university libraries.

TOXLINE
Free access to the National Library of Medicine's toxicology-specific database of abstracts, reference journal articles, and reports is available at http://www.medscape.com/misc/FormToxlineInfLive.html

MEDLINE

Free access to the National Library of Medicine's MEDLINE database of more than 9 million references to articles published in 3800 biomedical journals is available at http://www.nlm.nih.gov/databases/freemedl.html. Two Web-based products, PubMed and Internet Grateful Med, provide this access. Medline can also be accessed at http://www.medscape.com/misc/FormMedlineInfLive.html

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XYLENE (MIXED ISOMERS) (1330-20-7)

summary from the About the Chemicals section of Scorecard

- **Human Health Hazards**

  Recognized: --

Suspected:		Reference(s)
	Cardiovascular or Blood Toxicant	EPA-HEN RTECS
	Developmental Toxicant	EPA-HEN EPA-SARA JANK
	Gastrointestinal or Liver Toxicant	EPA-HEN RTECS
	Immunotoxicant	IPCS
	Neurotoxicant	DAN EPA-HEN OEHHA-2000 RTECS
	Reproductive Toxicant	EPA-SARA
	Respiratory Toxicant	EPA-HEN LU OEHHA-2000 OEHHA-AREL RTECS
	Skin or Sense Organ Toxicant	EPA-HEN OEHHA-AREL RTECS

- **Hazard Rankings**

  More hazardous than most chemicals in 3 out of 10 ranking systems.

- **Chemical Use Profile**

  This is a high volume chemical with production exceeding 1 million pounds annually in the U.S.
  Used in at least 12 industries.
  Used in consumer products, building materials or furnishings that contribute to indoor air pollution.
  Used in pesticide products.

- **Profile of Environmental Release and Waste Generation**

  For a list of the geographic areas, facilities, or industrial sectors which report the largest releases or transfers of this chemical to the Toxics Release Inventory, select what you want:

  - Rank States
  - Rank Counties
  - Rank Zip Codes
  - Rank Facilities
  - Rank Industrial Sectors

- **Regulatory Coverage**

  On at least 6 federal regulatory lists.

- **Basic Testing to Identify Chemical Hazards**

Eight basic tests to identify chemical hazards have been conducted and are publicly available for this chemical.

- **Information Needed for Safety Assessment**

  Lacks at least some of the national data required for safety assessment.
  Scorecard has risk assessment data for this chemical.

- **Links**

  Additional information about this chemical may be available elsewhere in Scorecard.

  Other web sites specific to this chemical:

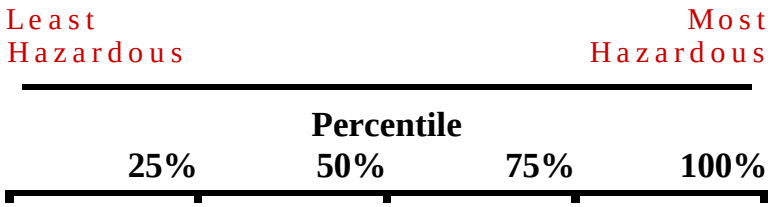
  - Agency for Toxic Substances and Disease Registry Public Health Statement
  - Agency for Toxic Substances and Disease Registry ToxFAQ
  - CalEPA Air Resources Board Toxic Air Contaminant Summary
  - EPA Health Effects Notebook for Hazardous Air Pollutants
  - EPA Integrated Risk Information System Report
  - EPA Office of Ground Water and Drinking Water Contaminant Fact Sheet
  - Environmental Writer Chemical Backgrounder
  - International Toxicity Estimates for Risk (ITER) from the Toxicology Excellence for Risk Assessment
  - National Toxicology Program Health and Safety Information Sheet

  If none of these sources meet your needs, you can try searching some other chemical database Web sites.

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Hazard Rankings

for XYLENE (MIXED ISOMERS) (1330-20-7) from Scorecard



Human Health Rankings

Toxicity only

- Ingestion Toxicity Weight (RSEI)
- Inhalation Toxicity Weight (RSEI)
- Human Health Effects Score (UTN)

Toxicity and exposure potential

- Noncancer Risk Score - Air Releases (EDF)
- Noncancer Risk Score - Water Releases (EDF)
- Worker Exposure Hazard Score (IRCH)

Ecological Health Rankings

Toxicity only

- Ecological Effects Score (UTN)

Toxicity and persistence

- Environmental Hazard Value Score (IRCH)

Integrated Environmental Rankings

Combined human and ecological scores

- Total Hazard Value Score (IRCH)
- Total Hazard Value Score (UTN)

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Industrial Uses

for XYLENE (MIXED ISOMERS) (1330-20-7) from Scorecard

This is a high volume chemical with production exceeding 1 million pounds annually in the U.S.

Which Industries Use This Chemical?	**How is the Chemical Used in This Industry?**
Electroplating	Electroplating - Cold-cleaning Solvents
Laboratory Chemicals	Solvents - Dilution
Machinery Mfg and Repair	Solvents - Machinery Manufacture and Repair
Paint Manufacture	Hydrocarbon Solvents
Paint Stripping	Solvents - Paint Stripping
Paper Coating	Solvents
Pesticide Mfg (Herbicides)	Solvents - Herbicide Manufacture
Pharmaceuticals Mfg	Solvents - Pharmaceuticals
Printing	Solvents for Gravure Printing
Rubber Manufacture	Solvents - Rubber Manufacture
Semiconductors	Developers - Negative
Wood Stains and Varnishes	Varnish Solvents

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Consumer Products

that contain XYLENE (MIXED ISOMERS) (1330-20-7) from Scorecard

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What kinds of consumer products may contain this chemical?

- Aerosol paint concentrates
- Agricultural chemicals
- Architectural coatings
- Auto, other transportation, and machinery refinish paints incl primers
- Automobile body polish and cleaners
- Caulks, modified and unmodified oil base
- Cooling tower compounds
- Epoxy adhesives
- Floor polish
- Fungicides for agric., garden and health service use
- General performance sealants (PVAC, butyl, vinyl, etc.)
- Ground/traffic marking coatings
- Herbicides for agric., garden and health service use
- Household hard surface cleaners (aerosol)
- Household hard surface cleaners (liquid)
- Household pesticides
- Industrial interior coatings
- Industrial particleboard (furniture, fixtures, cabinets, etc.)
- Insecticides for agric., garden and health service use
- Insecticides for crawling insects
- Insecticides for flying insects
- Lubricating oils
- Markers, fine point and broad tipped
- Misc. use aromatics
- Miscellaneous agricultural/pesticidal products
- Miscellaneous paint-related products
- Nonstructural caulking compounds and sealants
- Other art materials incl clay, water & tempera colors, finger paint, etc.
- Other automotive chemicals
- Other laundry aids, icluding ironing aids and dry cleaning spotting pre
- Other miscellaneous allied paint products, including brush cleaners
- Other nonhousehold pesticides

- Other polishing preparations and related products
- Other specialty cleaning and sanitation products
- Paint and varnish removers
- Paint thinners
- Paints and allied products
- Pet flea and tick products, including collars
- Preformed tapes (butyl, polybutene, polyisobutylene, etc.)
- Rodenticides
- Rubber and synthetic resin combinations
- Shoe polishes and cleaners
- Solvent thinned exterior stains incl shingle and shake
- Solvent thinned exterior undercoaters and primers
- Solvent thinned interior clear finishes
- Solvent thinned interior stains
- Solvent thinned interior undercoaters and primers
- Specialty performance sealants
- Synthetic resin and rubber adhesives
- Textile finishes
- Thick line coloring pens and markers
- Waterproofing compounds
- Wood office work surfaces (modular systems)

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Pesticidal Uses

for XYLENE (MIXED ISOMERS) (1330-20-7) from Scorecard

This is a high volume chemical with production exceeding 1 million pounds annually in the U.S.

List of Brand Name Products which Contain this Chemical	Percentage by Mass
AQUATIC WEED SOLVENT NO. 5-X	99%
AQUATIC WEED SOLVENT NO. 5-X	99%
AQUATIC WEED SOLVENT NO. 5-X	99%
WATER WEED KILLER	99%
AMOCO WATER WEED KILLER	99%
CROPMATE WATER WEED KILLER	99%
AQUA KLEER	98%
MALTER INTERNATIONAL OUT-CIDE	94.22%
BLACK MAGIC FORMULA D CONCENTRATED INSECTICIDE FOR ROACH CONTROL	90.1%
VITA PLUS MANGE WET TREATMENT FOR HOGS, CATTLE SHEEP.	90%
VAPO-FOG	90%
LAWN AND ORNAMENTAL GARDEN SPRAY	89.7%
LAWN AND ORNAMENTAL GARDEN SPRAY	89.7%
RID-SECT CONC RESIDUAL INSECTICIDE	89.39%
PATTERSON'S 5% LINDANE SPRAY	88%
GREEN LIGHT MANY PURPOSE SPRAY II	88%
BLACK MAGIC 555 ROACH SPRAY CONCENTRATE	87.5%
CLEAN CROP LINDANE 10% TRANSPLANTER SOLUTION	87%
METRO (TESTED) SOILDRIN D	86%
BEETLECIDE	85.3%
TWIN LIGHT ORGANIC SPRAY	85%
MOD-COM CONCENTRATED INSECTICIDE FOR FAST THOROUGH KILL	84.8%
CROWN LINDANE EMULSIFIABLE CONCENTRATE	84.39%
ROYAL BRAND BEETLE BUSTER	84%
ROYAL BRAND BEETLE BUSTER	84%
SUPER FLASH TOBACCO INSECTICIDE	83.63%
F-T-C-SPRAY	83.6%
GREEN UP LAWN & ORNAMENTAL INSECT SPRAY CONCENTRATE	83.35%

BEETLE-DED	83.3%
DIAZINON SPRAY MULTI-PURP INSECT SPRAY/LWN ORN.FLOWERS	83%
TIGER BRAND DEATH BLOW TOBACCO SPRAY	82.95%
ARNOLD SARCOPTIC MANGE TREATMENT	82.76%
FORMULA 267 PARCH NON-SELECTIVE HERBICIDE	82.59%
PRATT VEGETATION KILLER (CONTAINING PRAMITOL)	82.58%
PRATT VEGETATION KILLER (CONTAINING PRAMITOL)	82.58%
LINDANE E-1 INSECTICIDE	82.5%
SUPERSWEET MANGE & LICE CONTROL	82.5%
LIVESTOCK MANGE & LICE CONTROL	82.5%
LINDANE MANGE & LOUSE SPRAY	82.5%
LINDANE E-1 INSECTICIDE	82.5%
PCO LINDANE E-1 INSECTICIDE	82.5%
UNICORN LINDANE DOG DIP	82.11%
GREEN UP RED SPIDER MITICIDE	82%
GREEN UP RED SPIDER MITICIDE	82%
DE-PESTER DURSBAN E-1 INSECTICIDE	81.9%
CHEMTOX-BJ	81.71%
CHEMTOX-BJ	81.71%
UNICORN LINDANE MANGE & LOUSE SPRAY	80.5%
BEST 4 SERVIS BRAND DDVP 15% CONCENTRATE	80%
SO-PRO-CO- MALATHION 20	80%
GUTHION PARATHION .25-1	79.61%
GUTHION PARATHION .25-1	79.61%
GREEN UP DIAZINON SPRAY LAWN & GARDEN INSECT SPRAY	79.5%
SCIENCE FRUIT, NUT & GARDEN SPRAY	79.26%
ETHION-13% EMULSION	78.74%
NIAGARA NEW PRIME TOBACCO SPRAY	78.65%
STAA-CLEAR ABX	78.53%
LACCO HI-LIN	78.4%
CARL POOL CHINCH BUG KILLER	78%
MALLET	77.6%
STEPHENSON CHEMICALS 20% LINDANE EMULSIFIABLE CONCENTRATE	77%
INDUSTRIAL FORMULA 20% LINDANE	77%

GROWER SERVICE SUPERKILL TOBACCO SPRAY	76.86%
THIODAN-PARATHION 1-.5 E.C.	75.88%
THIODAN-PARATHION 1-.5 E.C.	75.88%
PROFESSIONAL NO. 20 LINDANE EMULSION CONCENTRATE	75%
B & B K-9 DIP CONCENTRATE FOR DOGS	75%
GOOD-WAY VAPONA INS. CONCENTRATE ANIMAL & AREA SPRAY	73.65%
ALL - MITEE EC	73%
CLARK SMITH'S GARDEN DOCTOR RX KELTHANE	73%
KELTHANE	73%
SUNNILAND KELTHANE EC	73%
PROKIL DICOFOL EC	73%
CARL POOL RED SPIDER SPRAY	73%
ROCKLAND "HOMEOWNER" KELTHANE MITICIDE	73%
KELTHANE EC	73%
KELTHANE EC	73%
SA-50 BRAND KELTHANE E.C.	73%
GREEN LIGHT RED SPIDER SPRAY + OTHER MITES	73%
UNICO **KELTHANE EMULSIFIABLE	73%
MITE-TROL	73%
SCIENCE KELTHANE EC	73%
BONIDE KELTHANE EC AGRICULTURAL MITICIDE	73%
MICHLIN MX-2 METHOXYCHLOR	72.9%
MICHLIN MX-2 METHOXYCHLOR	72.9%
BLACK LEAF LOGO GARDEN AND EVERGREEN SPRAY	72.6%
ANDERSON'S 181/2% DDVP CONCENTRATE	72.5%
TIDE THIODAN 2E	72.47%
KELTHANE SPRAY	72.4%
KELTHANE SPRAY	72.4%
EAGER BEAVER BRAND APHIS MILDEW SPRAY	72.15%
HACIENDA APHIS-MILDEW SPRAY	72.15%
NAVLET'S APHIS-MILDEW SPRAY	72.15%
COMBAT FARM AND GRAIN INSECTICIDE	72%
BLACK LEAF 25% METHOXYCHLOR	72%
SCIENCE 25% METHOXYCHLOR SPRAY	72%
SCIENCE 25% METHOXYCHLOR SPRAY	72%

FARMCRAFT LINDANE 2 EC	72%
LACCO LIN-O-SOL 20	72%
TWIN LIGHT METHOXYCHLOR SPRAY CONTAINS 2 LBS METHOXYCHLOR TECHNICAL PE	72%
E-Z-FLO METHOXYCHLOR 2 E	71.8%
METHOXYCHLOR EM-2 EMULSIFIABLE CONCENTRATE	71.8%
METHOXYCHLOR EM-2 EMULSIFIABLE CONCENTRATE	71.8%
HUB STATES METHOXYCHLOR 25-E EMULSIFIABLE CONCENTRATE	71.8%
METHOXYCHLOR EM-2 EMULSIFIABLE CONCENTRATE	71.8%
METHOXYCHLOR EM-2 EMULSIFIABLE CONCENTRATE	71.8%
PRENTOX METHOXYCHLOR 2# EMULSIFIABLE CONCENTRATE IN XYLENE	71.6%
VAPO MULSION 2	71.3%
MILLER THIODAN E.C. #2	71.3%
METHOXYCHLOR E-2	71%
METHOXYCHLOR E-2	71%
HELENA METHOXYCHLOR 2 E.C. INSECTICIDE	71%
METHOXYCHLOR E-2	71%
METHOXYCHLOR E-2	71%
E-Z FLO PRIME LEAF TOBACCO SPRAY INSECTICIDE	70.95%
PUREGRO THIODAN 2EC	70.7%
METHOXYCHLOR 25 EC	70.6%
HOPKINS METHOXYCHLOR EMULSIFIABLE CONCENTRATE	70.2%
DE-PESTER METHOXYCHLOR E-2	70%
BEST 4 SERVIS BRAND METHOXYCHLOR 25% EMULSIFIABLE SPRAY	70%
X-CEL KELTHANE EC MITICIDE	70%
ASGROW THIODAN 2 EMULSIVE	70%
PATTERSON'S GREEN UP RED SPIDER MITE SPRAY	70%
PATTERSON'S GREEN UP RED SPIDER MITE SPRAY	70%
TRIANGLE 25% METHYL PARATHION EMULSIFIABLE CONC.	70%
ORTHO METHOXYCHLOR 2 EMULSIVE	70%
DE-PESTER METHOXYCHLOR E-2	70%
GRO-TONE KELTHANE EC	70%
EN SURE EMULSIFIABLE CONCENTRATE INSECTICIDE	70%
MAGNOLIA DDVP-20 EMULSIFIABLE CONCENTRATE	70%

TRIANGLE 25% PARATHION EMULSIFIABLE CONCENTRATE	70%
ETHYL PARATHION 2 LB. CONCENTRATE	70%
BOUNTIFUL HARVEST MITE STOP	70%
E-Z FLO THIODAN 2 EC	70%
BEST 4 SERVIS BRAND ETHYL PARATHION 2 LB. CONCENTRATE	70%
DURSBAN E-2 INSECTICIDE	70%
METHOXYCHLOR 25 EC DYED SEED TREATER	69.8%
OCTAGON INSECTICIDE, METHOXYCHLOR EMULSIFIABLE CONCENTRATE	69.7%
PARATHION 2 LB. EMULSIFIABLE CONCENTRATE	69.58%
PARATHION 2 LB. EMULSIFIABLE CONCENTRATE	69.58%
PARATHION 2 LB. EMULSIFIABLE CONCENTRATE	69.58%
ROCKLAND TREE AND SHRUB SPRAY	69.5%
T-H THIODAN MISCIBLE WITH PYRENONE INSECTICIDE	69.02%
THIODAN MISCIBLE WITH PYRENONE	69.02%
SWIFT'S THIODAN MISCIBLE WITH PYRENONE	69.02%
WFSI THIODAN 2 E.C.	69%
EL BLANCO BRAND THIODAN 2 EC INSECTICIDE	69%
BRITZ BRAND THIODAN MISCIBLE PESTICIDE	69%
THIODAN 2-E EMULSIFIABLE CONC.	69%
THIODAN 2E	69%
OXY THIOSULFAN 2 EC INSECTICIDE	69%
THIODAN 2 EC	69%
MILLER'S THIODAN 2EC AGRICULTURAL INSECTICIDE	69%
GREEN LIGHT BORER KILLER	69%
SELCO THIODAN 2 LB. EMULSIFIABLE	69%
FCX THIODAN 2 "L"	69%
PEE GEE THIODAN MISCIBLE INSECTICIDE	69%
NACO THIODAN 2 E. C. INSECTICIDE	69%
THIODAN 2-E EMULSIFIABLE CONC.	69%
THIODAN TOBACCO SPRAY	69%
ENDOSULFAN INSECTICIDE	69%
FARMRITE THIODAN EC-2	69%
RED-TOP THIODAN 2 SPRAY	69%
THIODAN MISCIBLE INSECTICIDE	69%

EL BLANCO BRAND THIODAN 2 EC INSECTICIDE	69%
KAISER AGRICULTURAL CHEMICALS THIODAN MISCIBLE INSECTICIDE	69%
E-Z-FLO METHYL PARATHION 2 EMULSIVE	68.8%
GOLDCREST DULAK I	68.65%
GOLDCREST DULAK I	68.65%
SUPERIOR TURFBAN 2E	68.15%
SUPERIOR TURFBAN 2E	68.15%
THY-TOX 2E	68.1%
THY-TOX 2E	68.1%
DE-PESTER METHYL PARATHION E-2	68%
GRO-WELL PRO-TEK LIQUID INSECTICIDE	68%
SOILSERV THIODAN 25MS	67.9%
LINDANE BORER SPRAY	67.6%
D.D.V.P. 2# VAPONA	67.4%
TOBACCO SPRAY INSECTICIDE	67.2%
FCX THIODAN MALATHION TOBACCO SPRAY INSECTICIDE	67.2%
LINDANE 20% INSECTICIDE	66.85%
GREENUP LINDANE 20% CONCENTRATE	66.85%
PURINA RESIDUAL INSECT SPRAY	66.5%
GERMAIN'S GARDEN INSECT SPRAY	65.98%
THIODAN 2 PYRENONE 0.3-0.03 EC	65.8%
LINDANE BORER AND LEAF MINER SPRAY	65.6%
DURSBAN 21D INSECTICIDE	65.2%
PROFESSIONAL HEPTACHLOR 2E EMULSIFIABLE	64.9%
MICHLIN "MX-32" METHOXYCHLOR ELM TREE SPRAY INSECTICIDE	64.6%
MICHLIN "MX-32" METHOXYCHLOR ELM TREE SPRAY INSECTICIDE	64.6%
VAPONA INSECTICIDE EMULSIBLE CONCENTRATE	64.5%
PURINA VAPONA INSECT SPRAY CONCENTRATE	64.5%
SHELL BIDRIN INSECT EMUL CONC/PROF USE ONLY	64.45%
SHELL BIDRIN INSECT EMUL CONC/PROF USE ONLY	64.45%
NATIONAL CHEMSEARCH I-SO-SECT	64.4%
DIMITE 25% EMULSIFIABLE	64%
VAPONA INSECTICIDE	64%
SUPERIOR DURSBAN 2E	63.64%

WASCO METHOXYCHLOR 25% EMULSION CONCENTRATE	63%
E-Z-FLO CROP GUARD	63%
CHEMFORM BRAND LIQUID BARICIDE	63%
AGRISECT METHOXYCHLOR 25E	63%
E-Z-FLO CROP GUARD	63%
METHOXYCHLOR 25	63%
GABRIEL CHEMICALS LTD. METHOXYCHLOR 25 E	63%
METHOXYNON 2-1	63%
PROFESSIONAL HEPTACHLOR EMULSION CONCENTRATE	62.8%
DURSBAN - DDVP 2.50 TURF INSECTICIDE	62.42%
HELENA METHOCHLOR 3 E.C. INSECTICIDE	62%
PEE GEE HEPTACHLOR PRE-TREAT CONCENTRATE	61.36%
TOXO TOXODAN 3 EC	60.5%
TOXO TOXODAN 3 EC	60.5%
MORGRO FRUIT & BERRY SPRAY	60.45%
PRENTOX INSECT-MITE EMULSIFIABLE CONCENTRATE	60.3%
BEST 4 SERVIS BRAND METHYL PARATHION CONCENTRATE NO. 2	60%
E-Z FLO SUPERKILL PARATHION 1 THIODAN 2 EC	60%
CHECK-PEST B-20 LINDANE EMULSIFIABLE SPRAY CONC.	60%
E-Z FLO THIODAN 3 EC	59.7%
E-Z FLO THIODAN 3 EC	59.7%
AGWAY THIODAN 3E	59.7%
PARA-DAN SPRAY 1-2E	59.38%
METHO-D INSECTICIDE	59%
SMITH DOUGLASS THIODAN-PARATHION 2-1	58.36%
SMITH DOUGLASS THIODAN-PARATHION 2-1	58.36%
EMMY-1 "1-2" ETHYL & METHYL PARATHION	57.94%
ROTENONE 7 EC	57.6%
SMEAR SEAL SCREWWORM KILLER	57%
TERMINIX H3	56.9%
HACIENDA FRUIT AND VEGETABLE INSECT SPRAY	56%
PRATT MITE SPRAY CONTAINING KELTHANE FOR CLOVER MITES	56%
KELTHANE LIQUID CONCENTRATE MITE SPRAY	56%
KELTHANE LIQUID CONCENTRATE MITE SPRAY	56%
CROWN DZ-25 INSECTICIDE	56%

LINDANE 20 EMS	56%
CROWN DZ-25 INSECTICIDE	56%
BONIDE KELTHANE EC	56%
PROFESSIONAL GRADE DIAZINON INSECT SPRAY	55.9%
PROFESSIONAL GRADE DIAZINON INSECT SPRAY	55.9%
202K SHADE TREE INSECT SPRAY	55.4%
GUARDIAN ROBAN RESIDUAL INSECTICIDE	55%
TOBACCO STATES BRAND 20% LINDANE TRANSPLANTER SOLUTION	55%
EAGLE 2E CHLORPYRIFOS INSECTICIDE	54.8%
EAGLE 2E CHLORPYRIFOS INSECTICIDE	54.8%
PENPHENE	54.6%
LINDANE 20 MISCIBLE	54.5%
HOLIDAY HOLI-DIP	54.2%
METHYL PARATHION-THIODAN 1.5-1.5 EC	53.9%
OXY METHYL PARATHION-THIOSULFAN 1.5-1.5 EC	53.9%
PRATT'S 505K SHADE TREE INSECT SPRAY	51.17%
METHYL PARATHION CONCENTRATE NO. 4	51%
BLACK LEAF GARDEN & EVERGREEN SPRAY	50.85%
THREE-QUARTER-THREE EC COTTON INSECTICIDE	50.72%
GUTHION-MP .75-3 E.C.	50.72%
VEGETHION 45	50.31%
4 LB.METHYL PARATHION	50%
FORMULA MU-32 CYTHION INSECTICIDE FOGGING CONCENTRATE	50%
HELENA BRAND FOUR POUND METHYL PARATHION EMULSION	50%
HELENA BRAND METHYL PARATHION 4-EC	50%
THIODAN 50 W	50%
4.LB METHYL PARATHION EMULSIFIABLE INSECTICIDE CONCENTRATE	50%
GREEN UP 45% CHLORDANE EMULSIFIABLE CONCENTRATE	49.8%
45% CHLORDANE EMULSIFIABLE CONCENTRATE	49.8%
GREEN UP 45% CHLORDANE EMULSIFIABLE CONCENTRATE	49.8%
ALL-PURPOSE SYSTEMIC INSECTICIDE	49.6%
FARMINGDALE ALL-PURPOSE SYSTEMIC INSECTICIDE	49.6%
SMCP ENDOX NURSERY SPRAY	49.6%
PRO-BOLL M.P.-4 EMULSIFIABLE CONCENTRATE	49.52%

HELENA METHYL PARATHION 4-E	49.5%
METHYL PARATHION 4 LB. E. C.	49.5%
FCX METHYL PARATHION "4L"	49.5%
BEST 4 SERVIS BRAND PARATHION 4 LB. EMULSIFIABLE CONCENTRATE	49.32%
RING AROUND BRAND METHYL PARATHION 4# EMULSIFIABLE	49.19%
BRITZ BRAND PARATHION 4-EC	49%
PEE GEE E. P. 4 CONTAINS 4LBS. ETHYL PARATHION PER GALLON	49%
METADAN 2-2	49%
METADAN 2-2	49%
SURE KILL METHYL 4EC EMULISIFIABLE CONCENTRATE	49%
ATOMIC METHYL PARATHION 4E	48.8%
METHYL PARATHION 4 LB. EMULSIFIABLE LIQUID	48.7%
4 LB. METHYL PARATHION AN EMULS CONC INSECTICIDE FOR SPRAYING COTTON	48.63%
SFA BRAND 4 LB. METHYL PARATHION	48.47%
PARATHION 4 EC	48.4%
BEST PARATHION 4 EC	48.4%
METHYL PARATHION 4LB.	48.38%
TOBACCO STATES BRAND 2-M ALFALFA SPRAY	48.34%
VEGETHION 45	48.31%
RAVAP INSECTICIDE EMULSIFIABLE	48.3%
POULTRY LARVICIDE EMULSIFIABLE	48.3%
SHELL HORSE STABLE SPRAY EMULSIFIABLE CONCENTRATE	48.3%
POULTRY LARVICIDE EMULSIFIABLE	48.3%
SHELL HORSE STABLE SPRAY EMULSIFIABLE CONCENTRATE	48.3%
KENNEL AND YARD SPRAY CONCENTRATE	48.3%
PARATHION E-4	48.3%
PURINA RAVAP INSECTICIDE FOR RES. FLY CONTROL & MAGGOT KILLER	48.3%
POULTRY LARVICIDE EMULSIFIABLE	48.3%
RAVAP INSECTICIDE EMULSIFIABLE	48.3%
SHELL HORSE STABLE SPRAY EMULSIFIABLE CONCENTRATE	48.3%
RAVAP E.C. LIVESTOCK, POULTRY, PREMISE	48.3%
KENNEL AND YARD SPRAY CONCENTRATE	48.3%

BEST MALATHION METHOXYCHLOR 2-2 EC	48.3%
BEST MALATHION METHOXYCHLOR 2-2 EC	48.3%
FALL OUT PARATHION E-4	48.3%
PARATHION E-4	48.3%
RAVAP INSECTICIDE EMULSIFIABLE	48.3%
RAVAP E.C. LIVESTOCK, POULTRY, PREMISE	48.3%
YARD AND KENNEL FLEA AND TICK SPRAY CONCENTRATE	48.1%
DOUBLE-M ALFALFA SPRAY	48.1%
DELTA-4MP	48.01%
PUEBLO 4 LBS. ETHYL PARATHION E.C.	48%
CHAPMAN ETHYL PARATHION-4	48%
SIM-CHEM METHYL PARATHION 4-E	47.96%
SIM-CHEM METHYL PARATHION 4-E	47.96%
MISSION BRAND ETHYL PARATHION 4E.C.	47.7%
PARATHION 4-E	47.7%
NACO PARATHION 4 E INSECTICIDE	47.67%
SIM-CHEM PARATHION 4-E	47.54%
SIM-CHEM PARATHION 4-E	47.54%
METHYL PARATHION	47.5%
SURE DEATH BRAND 4LB. PARATHION EMULSTFLABLE	47.48%
FARM CHEM METHYL PARATHION 4E	47.46%
HELENA BRAND 4LB ETHYL PARATHION	47.3%
FASCO PARATHION 4 EC	47.15%
ALF-EX M-M ALFALFA SPRAY	47.1%
ETHIONE-4	47%
ETHIONE-4	47%
HOPKINS PARATHION 41B. PER GALLON E.C.	47%
ETHYL PARATHION 4-E. C.	47%
PLAINSMAN BRAND 4-E PARATHION	47%
TRIANGLE HEPTACHLOR 3 E.C. FOR TERMITE CONTROL	46.21%
AMOCO ALFALFA INSECTICIDE	46.1%
DE-PESTER METHYL PARATHION E-4	46%
FALL OUT METHYL PARATHION E-4	46%
DE-PESTER METHYL PARATHION E-4	46%
PARATHION 4 EMULSIVE	46%

TIDE ETHION 4E	45.81%
VAPONA FEEDLOT INSECTICIDE	45.8%
ETHION EMULSIFIABLE CONCENTRATE	45.74%
PURINA MANGE CONTROL	45.45%
FARNAM MANGE X	45.45%
DDVP 4 LB EMULSIFIABLE CONCENTRATE	45.35%
DDVP 4 LB EMULSIFIABLE CONCENTRATE	45.35%
DDVP 4 LB EMULSIFIABLE CONCENTRATE	45.35%
ALFALFA WEEVIL SPRAY	45.2%
49'ER GOLD STRIKE MALATHION-50	45%
ETHION 4 MISCIBLE MITICIDE INSECTICIDE	45%
HUB STATES 50% MALATHION EMULSIFIABLE SPRAY	45%
LIQUID 4E PARATHION	45%
THIONSPRAY NO.45	45%
FORVAP-4 VAPONA INSECTICIDE EMULSIFIABLE CONCENTRATE	45%
49'ER GOLD STRIKE MALATHION-50	45%
ETHION-4E	45%
THIONSPRAY NO.45	45%
ETHION-4E	45%
DAVIS "KILL-A-BUG"	44.89%
AGWAY T. M. FENTEX 4E	44.89%
NACO MALATHON METHOXYCHLOR 2-2 E. C.	44.82%
MALATHION 2-METHOXYCHLOR 2 EC	44.7%
MALATHION 2-METHOXYCHLOR 2 EC	44.7%
MALATHION 5 EMULSIVE	44.65%
HOPKINS ALFALFA AND CLOVER SPRAY 2-2 E.C.	44.63%
SHELL VAPONA INSECTICIDE EMULSIBLE CONCENTRATE	44.5%
CRYSTAL 4-LB METHYL PARATHION	44.5%
SHELL VAPONA INSECTICIDE EMULSIBLE CONCENTRATE	44.5%
SHELL VAPONA INSECTICIDE EMULSIBLE CONCENTRATE	44.5%
CRYSTAL 4-LB METHYL PARATHION	44.5%
CRYSTAL 4-LB METHYL PARATHION	44.5%
MALATHION METHOXYCHLOR 2-2 EC INSECTICIDE FOR USE ON ALFALFA	44.46%
GREENHOUSE CYTHION 50% INSECTICIDE	44%

PURINA VEGETABLE GARDEN INSECTICIDE	44%
GREENHOUSE CYTHION 50% INSECTICIDE	44%
EAGLE DIAZINON 4S INSECTICIDE	43.8%
EAGLE DIAZINON 4S INSECTICIDE	43.8%
M & M	43.65%
SMITH-DOUGLASS IMANEM ALFALFA WEEVIL INSECTICIDE	43.51%
SMITH-DOUGLASS IMANEM ALFALFA WEEVIL INSECTICIDE	43.51%
CO-OP ALFA-CIDE	43.51%
SURE DEATH BRAND M-M-4	43.51%
MOSQUITO SPRAY	43.51%
ALFA - SPRAY	43.51%
ALFA-GARD	43.51%
SUDBURY MALATHION LIQUID CONCENTRATE INSECT SPRAY	43.3%
SUDBURY HOUSEHOLD INSECT SPRAY FOR OUTDOOR USE	43.3%
SUDBURY MALATHION LIQUID CONCENTRATE INSECT SPRAY	43.3%
SUDBURY HOUSEHOLD INSECT SPRAY FOR OUTDOOR USE	43.3%
DR. ROGER'S MALATHION - 50	43%
DR. ROGER'S MALATHION - 50	43%
HERITAGE HOUSE 50% MALATHION INSECT SPRAY	42.8%
GRO-WELL 50% MALATHION SPRAY	42.4%
LEBANON GARDEN SPRAY CONTAINS 50% MALATHION	42.4%
TWIN LIGHT MALATHION 50% SPRAY	42.4%
50% MALATHION SPRAY	42.37%
50% MALATHION SPRAY	42.36%
STATEBRAND FORMULA 262 MX-50 INSECTICIDE	42%
TASCO BRAND 50% MALATHION EMULSION CONCENTRATE	41.9%
PURINA MALATHION SPRAY (PREMIUM GRADE)	41.8%
SCREW WORM SMEAR	41.69%
SMITH-DOUGLASS MALATHION 50% EMULSION CONCENTRATE	41.37%
SMITH-DOUGLASS MALATHION 50% EMULSION CONCENTRATE	41.37%
ROCKLAND MALATHION 50% EMULSIFIABLE CONCENTRATE	40.8%
FOR-MAL 50 50% MALATHION E.C.	40.37%
PRENTOX MALATHION 57% PREMIUM GRADE EMULSIFIABLE INSECTICIDE	40%
DDVP 50% EMULSIFIABLE CONCENTRATE	40%

CHEMFORM BRAND MALATHION EMULSIFIABLE CONCENTRATE	40%
GREEN UP DIAZINON 500 INSECTICIDE	40%
MALATHION 57%	40%
HAHN'S FLWR SHRB TREE SPRY MALATHION WE EMULS CONC 50%	40%
DDVP 50% EMULSIFIABLE CONCENTRATE	40%
AIDEX MALATHION PREMIUM-5S	40%
DDVP 50% EMULSIFIABLE CONCENTRATE	40%
DIAZINON AG-4 INSECTICIDE	39.8%
RED-TOP ABATE 4 SPRAY	39.8%
DIAZINON AG-4 INSECTICIDE	39.8%
D-TOX-AG-500 INSECTICIDE	39.6%
NACO DIAZINON AG 500 INSECTICIDE	39.54%
DIZON 4 S INSECTICIDE	39.5%
DIZON 4 S INSECTICIDE	39.5%
AGCO BRAND METHYL PARATHION 4 INSECTICIDE	39.5%
SMITH DOUGLS MAL 4.5 EMULS CONC.LIQUID AGR. INSECTICIDE	39.49%
SMITH DOUGLS MAL 4.5 EMULS CONC.LIQUID AGR. INSECTICIDE	39.49%
METHYL PARATHION 5-E	39.42%
DIAZINON AG 500 INSECTICIDE	39.4%
STEPHENSON CHEMICALS HEPTACHLOR 4 LB. E.C.	39.4%
LACCO DIAZINON AG 500 INSECTICIDE	39.4%
CYTHION INSECTICIDE	39.1%
SMITH-DOUGLASS DIAZINON INSECTICIDE AG500	39.02%
SMITH-DOUGLASS DIAZINON INSECTICIDE AG500	39.02%
DIAZINON 500 EC	39%
MALATHION EC	39%
DIAZINON 500 EC	39%
INDUSTRIAL FORMULA MALATHION 50% EMULSIFIABLE CONCENTRATE	39%
PREMIUM GRADE MALATHION INSECT SPRAY 50%	39%
DIAZINON AG 500	39%
GREEN LIGHT TOMATO & VEGETABLE SPRAY CONCENTRATE	39%
DIAZINON AG-4 INSECTICIDE	39%
MILLER DIAZINON AG INSECTICIDE	38.96%
BAC DIAZINON 4E	38.96%

DIAZINON 4-EC	38.8%
AGCO DIAZINON AG500	38.7%
FLYGON 2-E SYSTEMIC INSECTICIDE	38.4%
FALLOUT MALATHION 5	38.38%
TIDE MALATHION 5-PGE EMULSIFIABLE LIQUID	38.38%
NACO METHYL PARATHION 4 E C INSECTICIDE	38.18%
UNICO SUPERIOR KILLA-DILLA TOBACCO SPRAY	38.1%
BEST 4 SERVIS BRAND PREMIUM 57% MALATHION GRAIN PROTECTOR EMULSIFI	38%
BEST 4 SERVIS BRAND METHYL PARATHION CONCENTRATE NO. 4	38%
DIAZINON AG 500 E-Z-FLO AGRICULTLTURAL	38%
DIAZINON AG 500 E-Z-FLO AGRICULTLTURAL	38%
DIAZINON 4E	38%
DIAZINON 4 EC	38%
HAYNES + MORGAN GRAIN BIN SPRAY	38%
MALATHION - 50 - SPRAY	38%
GOOD-LIFE 57% MALATHION LIQUID	37.64%
CROP KING MALATHION 5-E	37.5%
CROP KING MALATHION 5-E	37.5%
METHYL PARATHION 4E	37.12%
METASPRAY 4-1 EC	37%
57% MALATHION (PREMIUM GRADE)	37%
ORTHO METHYL PARATHION 5 EMULSIVE	37%
METASPRAY 4-1EC	37%
AMOCO MALATHION SPRAY	37%
CIBA-GEIGY METHIDATHION 60S	36.8%
CHIPMAN DIAZOL 50E	36.58%
MALATHION 50% CONCENTRATED EMULSION	36.5%
GRO MALATHION 50% CONCENTRATED EMULSION	36.5%
LILLY/MILLER ROSE & EVERGREEN INSECT SPRAY	36.4%
ETHION EM-4 EMULSIFIABLE CONCENTRATE	36.1%
ETHION EM-4 EMULSIFIABLE CONCENTRATE	36.1%
KITTEN & BEAR BRAND KAYAZINON AG-500	36%
KITTEN & BEAR BRAND KAYAZINON AG-500	36%
DIAZINON AG 500	36%

ATLANTIC DIAZINON AG-500	36%
DIAZINON AG500	36%
TOBACCO STATES BRAND DIAZINON AG-500 INSECTICIDE	36%
DIAZINON R 4 EC	36%
PRATT DIAZINON AG 4E FOR TURF AND TREE	36%
PUREGRO DIAZINON AG500	36%
MALATHION EMULSIFIABLE	36%
FASCO DIAZINON AG 500	36%
DIMP 4 EC	36%
TIDE DIAZINON AG 500	36%
DIAZINON 4 E.C.	36%
DIAZINON AG500 INSECTICIDE	36%
DIAZOL DIAZINON 4 LBS. PER GAL AGRICULTURAL OIL CONCENTRATE	36%
DIAZINON 4 EC	36%
DIAZINON 4 EC	36%
FALL OUT DIAZINON AG 500	36%
PROFESSIONAL PEST CONTROL FORMULA DC-500	36%
EAGLE DIAZINON AG500 INSECTICIDE	36%
DIAZINON AG500	36%
DIAZINON AG500	36%
DIAZINON AG500	36%
MULTI - PURPOSE EMULSIFIABLE MALATHION	35.82%
MULTI - PURPOSE EMULSIFIABLE MALATHION	35.82%
NACO PREMIUM GRADE MALATHION 5 EC	35.53%
CYTHION 5 EC	35.5%
BEST 50% MALATHION INSECT SPRAY	35.4%
PROFESSIONAL GRADE MALATHION INSECT SPRAY	35.4%
FCX FARM CHEMICALS MALATHION-5 EMULSIFIABLE CONCENTRATE	35.4%
FCX CYTHION 5	35.4%
KILL A PLENTY PREMIUM MALATHION	35.3%
HEPTACHLOR 2 LB EMULSIFIABLE CONCENTRATE	35.24%
GOODLIFE MALATHION 5	35.19%
GOOD-LIFE MALATHION 57% PREMIUM	35.1%
GOOD-LIFE MALATHION 57% PREMIUM	35.1%

MALA MULSION 5	35%
REDWOOD'S 57% MALATHION EMULSIFIABLE CONCENTRATE	35%
RUSSELL 56% MALATHION EMULSIFIABLE CONCENTRATE	35%
RESIDEX MALATHION 5 LB., 57% (PREMIUM GRADE) EMULSIFIABLE CONCENTRATE	35%
MALA MULSION 5	35%
FARM BUREAU CO-OP 57% MALATHION EMULSIFIABLE CONCENTRATE	35%
M 4 F MURDER FOR FLIES	35%
SURE DEATH BRAND MALATHION W-E	35%
WOODBURY'S MALACIDE GRAIN PROTECTANT	35%
RED-TOP METHYL PARATHION 2 THIODAN 3 SPRAY	35%
CARMEL FORMULA MU-25 CYTHION EMULSIFIABLE CONCENTRATE	35%
57% MALATHION EMULSIFIABLE CONCENTRATE	35%
HERITAGE HOUSE FRUIT, NUT AND VEGETABLE SPRAY	35%
MALATHION 55	35%
PROFESSIONAL 57% MALATHION	35%
E-Z-FLO CYTHION	35%
DE-PESTER MALATHION 50% EC	35%
DE-PESTER PREMIUM MALATHION E-5	35%
BRULIN EM-50	35%
STEPHENSON CHEMICALS HEPTACHLOR 2 LB. E.C.	34.6%
UNICO ROSE LOX CONTAINS META-SYSTOX R SYSTEMIC INSECTICIDE	34.5%
MOSQUITO FOGGING CONCENTRATE	34.5%
DURSBAN 6	34.5%
SUPER MALLET	34.1%
AIDEX MALATHION PREMIUM 5E	34%
PIONEER BRAND 56% MALATHION EMULSIFIABLE CONCENTRATE	34%
PIONEER BRAND 57% MALATHION EMULSIFIABLE LIQUID	34%
PIONEER BRAND GRAIN GARD PREMIUM 57% MALATHION	34%
NOVA MALATHION 57-WE	34%
MAL-O-SECT	34%
RED BARN MALATHION 5P	34%
AIDEX MALATHION PREMIUM 5E	34%

EMMY 2 2-3 ETHYL & METHYL PARATHION	33.65%
FARMCHEM MALATHION 5E	33.5%
CO-OP CYTHION 5E THE PREMIUM GRADE MALATHION	33.5%
CO-OP CYTHION 5E THE PREMIUM GRADE MALATHION	33.5%
LACCO MALA MULSION 5	33.46%
LACCO MALA MULSION 5	33.46%
FORMULA 57	33.09%
ELITE MALATHION 50% E.C.	33%
THIODAN METHYL PARATHION 3-2-E.C.	33%
RING AROUND BRAND 5# MALATHION EMULSIFIALBE	33%
MALATHION GRAIN PROTECTANT	33%
NACO MALATHION 5 EMULSION	33%
BAYGON MOS INSECTICIDE	33%
PARATHION SOIL TREATED	33%
CYBROM - E.C.	32.4%
TERMINIX GP-MAL CONCENTRATE	32.2%
TERMINIX GP-MAL CONCENTRATE	32.2%
T-H CYTHION PREMIUM GRADE MALATHION E-5	32%
MASTER BRAND LIVESTOCK SPRAY	32%
TIFCHEM 57% MALATHION EMUL. CONCENTRATE	32%
HI BRAND MALATHION E-5	32%
KAISER AGRICULTURAL CHEMICALS CYTHION FOR STORED GRAIN	32%
FOR-MAL 57 5 LBS. PREMIUM GRADE MALATHION PER GALLON	32%
TRIPLE ACTION KNOCK DOWN QUICK KILL RES KILL PRE. GRADE MALATHION	32%
STEPHENSON'S PREMIUM GRADE MALATHION FOR STORED GRAIN	32%
TOBACCO STATES BRAND 57% MALATHION EMULS. CONC.CONT.PR.	32%
SWIFT'S SUPER GUARD 57% MALATHION EMULSIFIABLE CONCENTRATE	32%
E-Z-FLO 57% MALATHION EC	32%
MALACOAT	32%
PLAINSMAN MALATHION EMULSIFIABLE CONCENTRATE	32%
UNICO MALATHION GRAIN SPRAY PREMIUM GRADE	32%
FCX MALATHION GRAIN SPRAY	32%
57% MALATHION E. C. PREMIUM GRADE	32%

MASTER BRAND LIVESTOCK SPRAY	32%
LYSTAD'S D-M SPRAY FOR DRY MILK PLANTS AND BOX CARS	32%
TIGER BRAND MALATHION	32%
PREMIUM GRADE MALATHION FOR STORED PEANUTS	32%
57% PERMIUM GRADE MALATHION	32%
T-H CYTHION PREMIUM GRADE MALATHION E-5	32%
CYTHION 5 E. C.	32%
TOBACCO STATES BRAND 57% MALATHION EMULS. CONC.CONT.PR.	32%
TOBACCO STATES BRAND 57% MALATHION EMULS. CONC.CONT.PR.	32%
SPECIAL GRADE METASPRAY 5E	31.88%
GRAIN PROTECTION SPRAY	31.5%
P.T.O. MALATHION 57% E.C.	31.4%
TPC GRAIN PROTECTANT 5LB MALATHION EMULS CONC PREM GR.	31%
CYTHION 5 EC FOR MOSQUITO CONTROL	30.7%
PRENTOX METHOXYCHLOR 3# EMULSIFIABLE CONCENTRATE	30.7%
CHLORPYRIFOS SPECIAL MIXTURE NO1	30.2%
BIO SERV DIAZINON 4 LB	30.1%
FARNAM DIP QUICK-M	30%
HOPKINS MALATHION 57% EMULSIFIABLE LIQUID INSECTICIDE	30%
CYTHION 57 INSECTICIDE PREMIUM GRADE MALATHION	30%
SOILSERV THIODAN-PARATHION 2-1 EC	30%
THE BUG HOUSE 57% MALATHION EMULSIFIABLE CONCENTRAT	30%
SOUTHLAND 57% MALATHION	30%
57% MALATHION	30%
CYTHION 57% EC	30%
PHILLIPS 66 MILLER KILLER	29.5%
57% MALATHION	28.83%
TPC AN-I-MAL SPRAY	28%
MALACIDE CONCENTRATE	28%
THIODAN-METHYL PARATHION 2-1 EC	28%
TPC MALGORA SPRAY	28%
TPC AN-I-MAL SPRAY	28%
DISULFOTON LIQUID CONCENTRATE INSECTICIDE	27%
METHYL PARATHION 5 EC	26.4%
BEST METHYL PARATHION 5 EC	26.4%

EAGLE DIAZINON 4E INSECTICIDE	26.2%
DIZON 4E INSECTICIDE	26.2%
EAGLE DIAZINON 4E INSECTICIDE	26.2%
GUARDIAN MALATHION OIL SOLUBLE 50% (NO. 6201)	25%
PURINA POULTRY INSECTICIDE	25%
BAC PARATHION 4E	24.6%
CHAMPION CHLORDANE 75% EMULSIFIABLE CONCENTRATE	24%
FORBAN 4 EMULSIFIABLE INSECTICIDE CONCENTRATE	23.7%
B & G DURSBAN 4E EMULSIFIABLE INSECTICIDE	23.7%
SUPERIOR DURSBAN 4E EMULSIFIABLE CONCENTRATE	23.7%
METHYL PARATHION 5 EC	23.6%
HELENA BRAND CHLORDANE 8-E AN EMULSIFIABLE INSECTICIDE LIQUID	22.5%
SOILSERV DIBROM 8EC	22.3%
RING AROUND BRAND K0-THION	22.23%
EAGLE 4E CHLORPYRIFOS INSECTICIDE	22%
RIVERSIDE 74% CHLORDANE EMULSIFIABLE	22%
EAGLE 4E CHLORPYRIFOS INSECTICIDE	22%
72% CHLORDANE EMULSIFIABLE CONCENTRATE	22%
GREEN UP 72% CHLORDANE	22%
NACO CHLORDANE 8 EC INSECTICIDE	21.07%
METHOXYCHLOR EMULSIFIABLE CONCENTRATE	21%
GUTHION PLUS METHYL PARATHION SPRAY CONC	20.5%
TOXO DIBROM* EMULSIFIABLE NO.8	20%
DIBROM 8E	20%
COASTOX DIBROM 8 EMULSIVE	20%
BAC NALBROM EMULSIVE	20%
ORTHO DIBROM 8 EMULSIVE	20%
DIBROM 8 EC	20%
METRO(TESTED) ROSE STEMIC DUAL GARDEN SPRAY	20%
FASCO DIBROM 8EC	20%
WES-GRO BRAND DIBROM 8 EMULSIVE	20%
BRITZ BRAND DIBROM 8 EMULSIVE NALED INSECTICIDE	20%
DIBROM R 8 EMULSIVE	20%
WFSI DIBROM 8 EMULSIVE	20%

DIBROM 8 EC	20%
TOXO DIBROM* EMULSIFIABLE NO.8	20%
DIBROM R 8 MISCIBLE	20%
THIODAN 2 C.O. EC	20%
LEFFINGWELL DIBROM 8 EMULSIVE NALED INSECTICIDE	20%
LEFFINGWELL DIBROM 8 EMULSIVE NALED INSECTICIDE	20%
PUREGRO DIBROM 8 EMULSIVE NALED INSECTICIDE	20%
DIBROM 8 EC	20%
FASCO DIBROM 8 EC	20%
CARMEL FORMULA MU-23	20%
BIO-SEC 8X	20%
DIBROM 8E	20%
DIBROM 8 EC NALED INSECTICIDE	20%
WOODLIFE MILLTREAT TYPE E CONCENTRATE	19.6%
DIAZINON 4E FORSHAW BRAND INSECTICIDE	19.25%
METHYL PARATHION 7.5 EC	18.4%
METHYL PARATHION 7.5 EC	18.4%
METHYL PARATHION	18%
THIODAN PYRENONE C.O. EC	18%
72% CHLORDANE EMULSIFIABLE CONCENTRATE	17.8%
PRENTOX METHYL PARATHION TECHNICAL	17%
PRENTOX METHYL PARATHION TECHNICAL	17%
MIL-P 19451A	16.5%
PENTA-40	15.6%
ELITE FLEA AND TICK DIP II	15%
UNICORN LINDANE SCREW WORM SPRAY	15%
BAC MALATHION SPRAY 8-E	14.38%
ISOTOX TRANSPLANTER SOLUTION	14.2%
ZEMA FLEA & TICK DIP	14%
METHYL DEMOX 2 LBS. /GALS.	14%
SYSTEMIC SPRAY CONCENTRATE INSECTICIDE	14%
METRO (TESTED) METRO STEMIC GARDEN SPRAY	14%
BONIDE SYSTEMIC INSECT SPRAY	14%
SCREW-WORM EAR-TICK BOMB	12.5%
OSBORN SW-T BOMB	12.5%

SCREW-WORM EAR TICK SPRAY	12.5%
FOUR WAY SECREW WORM SPRAY	12.5%
METHYL PARATHION 80 STABILIZED	12.5%
FARNAM SCREW WORM EAR TICK BOMB II	12.5%
ZEMA D	12%
INSECTICIDE LINDANE EMULSIFIABLE 12%	12%
SQUERM-JET	12%
PLAINSMAN BRAND 8-WE PARATHION	12%
KIL-A-MITE	12%
EMTHION 4-4	11.91%
RING AROUND BRAND M-M 4-4 INSECTICIDE	11.39%
AGRISECT PARATHION 8E	11.2%
EAGER BEAVER BRAND FRUIT-VEGETABLE INSECT SPRAY	11%
THIMET 600 SYSTEMIC INSECTICIDE	11%
HACIENDA FRUIT AND VEGETABLE INSECT SPRAY	11%
NAVLET'S FRUIT AND VEGETABLE INSECT SPRAY	11%
M. A. D. SPECIAL MOSQUITOCIDE	10.5%
EAR TICK REMEDY	10.5%
SOILSERV METAPHOS 50	10.4%
BRITZ BRAND METHYL PARATHION 5 EMULSIVE (INSECTICIDE)	10%
GUARDIAN PYRETHRIN EMULSIFIABLE CONCENTRATE PRODUCT NO. 6603	10%
BENZYL-DEX	10%
SMEAREX 367	10%
BENZYL-DEX L	10%
PARATHION 8LB. E.C.	9.91%
PARATHION 8LB. E.C.	9.91%
PARATHION 8E	9.1%
FARMCHEM PARATHION 8E	9.03%
E-Z-FLO PARATHION 8-E	9.03%
SCREW WORM AND EAR TICK SPRAY	8.94%
PARATHION 8 CONCENTRATE	8.78%
PARATHION 8E	8.78%
OLIN-MMP- 63 ULV INSECTICIDE FOR USE ON COTTON	8%
OLIN-MMP- 63 ULV INSECTICIDE FOR USE ON COTTON	8%

OLIN-MMP- 63 ULV INSECTICIDE FOR USE ON COTTON	8%
PUEBLO 8 LB. PARATHION-MISCIBLE E.C.	7.9%
PUEBLO 8 LB. PARATHION-MISCIBLE E.C.	7.9%
MALATHION SPRAY NO 8-E	7.7%
MALATHIM SPRAY 8E	7.7%
MALA MULSION 8	7.65%
MALA MULSION 8	7.65%
ETHYL METHYL PARATHION 6-3 EC	6.5%
ETHYL METHYL PARATHION 6-3 EC	6.5%
EMTHION 6:3	6.44%
AGRO-CHEM BRAND PAIR EM 6-3	6.44%
PURE GRO ETHYL-METHYL PARATHION 6-3E	6.44%
AGWAY PARATHION 8 EC	6.2%
AGCO BRAND PARATHION 8 INSECTICIDE	6.2%
CYGARD 630 INSECTICIDE	6.2%
CYAGRD 630	6.2%
BEST 4 SERVIS BRAND FLIGHT PARATHION CONCENTRATE	6%
B & G DURSBAN 1E EMULSIFIABLE INSECTICIDE	5.9%
T CHEM PARATHION 8 LB. EMULSION CONCENTRATE	5.8%
PINCHER	5.8%
AIDEX MALATHION 90% PREMIUM O.S.	5.26%
AIDEX MALATHION 90% PREMIUM O.S.	5.26%
BAC CYTHION	5%
MALATHION 8LB. EC	5%
MALATHION 8LB. CONCENTRATE	4.29%
MALATHION 8LB. CONCENTRATE	4.29%
PARASITE CONTROL CATTLE OIL	3%
DALE'S HOG & CATTLE OIL	3%
PRENTOX ETHYL PARATHION TECHNICAL	3%
PAMLINE BEEF CATTLE OIL NO. 2006	3%
PRENTOX ETHYL PARATHION TECHNICAL	3%
PAMLINE BEEF CATTLE OIL NO. 2006	3%
MALATHION 82% EMULSIFIABLE CONCENTRATE INSECTICIDE	3%
MALATHION PREMIUM GRADE 82% EMULSIFIABLE CONCENTRATE INSECTICIDE	3%

MALATHION 82-E INSECTICIDE	3%
STOCHINE CATTLE OIL (MALATHION)	3%
SCHAEFFER'S NO.1 BEEF CATTLE + HOG OIL	3%
HUB STATES VAPONA AEROSOL INSECTICIDE	2%
RILEY BROS. BACK RUBBER OIL	2%
MALATHION E-8	1.6%
DE-PESTER MALATHION E-8	1.6%
DE-PESTER MALATHION E-8	1.6%
MALATHION E-8	1.6%
AIDEX 2% MALATHION	1.3%
ALL-SEASON LIVESTOCK OIL	1.3%
AIDEX 2% MALATHION	1.3%
CURRY-TROL OIL FOR USE ON DAIRY CATTLE AIDS IN THE CONTROL OF LICE	1%
CURRY-TROL OIL	.5%
ATLAS 701 NOX-AL RESIDUAL ROACH & INSECT SPRAY	.38%

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States with Reported Total Environmental Releases

of XYLENE (MIXED ISOMERS) (1330-20-7) from the About The Chemicals section of Scorecard

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Ranked by (select your ranking criteria)

Total environmental releases Go (explain)

1. MICHIGAN: 7,723,868 Pounds
2. TEXAS: 5,265,725 Pounds
3. INDIANA: 4,759,069 Pounds
4. OHIO: 4,235,512 Pounds
5. MISSOURI: 3,637,501 Pounds
6. GEORGIA: 3,232,144 Pounds
7. TENNESSEE: 3,088,480 Pounds
8. ILLINOIS: 2,635,402 Pounds
9. ALABAMA: 2,481,030 Pounds
10. KENTUCKY: 2,329,514 Pounds
11. KANSAS: 2,076,366 Pounds
12. PENNSYLVANIA: 1,960,219 Pounds
13. MINNESOTA: 1,957,104 Pounds
14. MISSISSIPPI: 1,956,838 Pounds
15. IOWA: 1,951,132 Pounds
16. WISCONSIN: 1,919,345 Pounds
17. VIRGINIA: 1,831,068 Pounds
18. LOUISIANA: 1,480,085 Pounds
19. ARKANSAS: 1,290,305 Pounds
20. OKLAHOMA: 1,252,053 Pounds
21. NEW JERSEY: 1,198,079 Pounds
22. SOUTH CAROLINA: 973,299 Pounds
23. NEBRASKA: 863,685 Pounds
24. FLORIDA: 857,863 Pounds
25. CALIFORNIA: 841,512 Pounds
26. NEW YORK: 822,977 Pounds
27. NORTH CAROLINA: 777,580 Pounds
28. MARYLAND: 625,357 Pounds

29. WEST VIRGINIA: 606,733 Pounds
30. SOUTH DAKOTA: 579,402 Pounds
31. WASHINGTON: 486,568 Pounds
32. OREGON: 426,652 Pounds
33. DELAWARE: 300,936 Pounds
34. NEW HAMPSHIRE: 299,547 Pounds
35. MASSACHUSETTS: 256,097 Pounds
36. NEW MEXICO: 250,312 Pounds
37. IDAHO: 219,471 Pounds
38. UTAH: 200,003 Pounds
39. NORTH DAKOTA: 153,679 Pounds
40. VIRGIN ISLANDS: 120,665 Pounds
41. CONNECTICUT: 119,635 Pounds
42. RHODE ISLAND: 108,377 Pounds
43. WYOMING: 102,815 Pounds
44. PUERTO RICO: 97,413 Pounds
45. MONTANA: 70,025 Pounds
46. ALASKA: 67,602 Pounds
47. COLORADO: 64,547 Pounds
48. ARIZONA: 42,927 Pounds
49. NEVADA: 42,290 Pounds
50. HAWAII: 19,864 Pounds
51. MAINE: 18,377 Pounds
52. VERMONT: 2,143 Pounds
53. AMERICAN SAMOA: 524 Pounds
54. GUAM: 328 Pounds
55. NORTHERN MARIANA ISLANDS: 11 Pounds

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Counties with Reported Total Environmental Releases

of XYLENE (MIXED ISOMERS) (1330-20-7) from the About The Chemicals section of Scorecard

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Ranked by (select your ranking criteria)

Total environmental releases

in

Entire United States Go (explain)

1. WAYNE, MI: 1,560,474 pounds
2. KENT, MI: 1,369,799 pounds
3. DEKALB, GA: 1,262,491 pounds
4. CLAY, MO: 1,226,362 pounds
5. TARRANT, TX: 1,045,468 pounds
6. COOK, IL: 951,878 pounds
7. GENESEE, MI: 837,155 pounds
8. JEFFERSON, KY: 836,297 pounds
9. ALLEGAN, MI: 823,997 pounds
10. ST. LOUIS, MO: 815,358 pounds
11. HARRIS, TX: 787,543 pounds
12. WYANDOTTE, KS: 773,502 pounds
13. OAKLAND, MI: 772,234 pounds
14. TIPPECANOE, IN: 749,747 pounds
15. MACOMB, MI: 660,906 pounds
16. LOWNDES, MS: 625,114 pounds
17. ALLEN, IN: 611,440 pounds
18. LUCAS, OH: 529,641 pounds
19. MIDDLESEX, NJ: 525,379 pounds
20. UNION, OH: 509,100 pounds
21. OKLAHOMA, OK: 480,999 pounds
22. NORFOLK (CITY), VA: 471,880 pounds
23. SHERBURNE, MN: 464,258 pounds
24. JEFFERSON, TX: 444,859 pounds
25. JEFFERSON, AL: 432,413 pounds

26. BALTIMORE (CITY), MD: 414,032 pounds
27. TRUMBULL, OH: 403,391 pounds
28. RAMSEY, MN: 401,910 pounds
29. FULTON, GA: 389,209 pounds
30. BROOKE, WV: 387,352 pounds
31. WICHITA, TX: 375,484 pounds
32. OSCEOLA, MI: 369,000 pounds
33. SCOTT, KY: 365,469 pounds
34. ST. CHARLES, MO: 362,010 pounds
35. LORAIN, OH: 360,843 pounds
36. SCHENECTADY, NY: 350,802 pounds
37. INGHAM, MI: 343,981 pounds
38. BROWN, TX: 341,701 pounds
39. RUTHERFORD, TN: 318,535 pounds
40. LAUDERDALE, TN: 317,850 pounds
41. ROCK, WI: 317,730 pounds
42. DUBOIS, IN: 312,054 pounds
43. ROBERTSON, TN: 311,550 pounds
44. NUECES, TX: 305,028 pounds
45. MONROE, MI: 304,866 pounds
46. ELKHART, IN: 303,526 pounds
47. CALCASIEU, LA: 301,902 pounds
48. HALL, NE: 300,000 pounds
49. BAY, FL: 295,368 pounds
50. MILWAUKEE, WI: 292,217 pounds
51. NEW CASTLE, DE: 290,616 pounds
52. WINSTON, AL: 288,764 pounds
53. MULTNOMAH, OR: 284,467 pounds
54. LOS ANGELES, CA: 278,369 pounds
55. ALLEGHENY, PA: 275,390 pounds
56. MERCER, OH: 256,657 pounds
57. SUMTER, GA: 253,057 pounds
58. CUYAHOGA, OH: 252,051 pounds

59. SEBASTIAN, AR: 247,965 pounds
60. ROCKINGHAM, NH: 242,434 pounds
61. LANCASTER, PA: 236,969 pounds
62. DAKOTA, MN: 234,586 pounds
63. SULLIVAN, TN: 230,610 pounds
64. MARION, AL: 229,907 pounds
65. LEE, MS: 226,345 pounds
66. DOUGLAS, NE: 215,997 pounds
67. VERNON, MO: 213,300 pounds
68. JASPER, IA: 212,080 pounds
69. BARRY, MO: 209,782 pounds
70. SEDGWICK, KS: 209,275 pounds
71. PORTER, IN: 208,329 pounds
72. HENRICO, VA: 201,866 pounds
73. PEORIA, IL: 201,294 pounds
74. CADDO, LA: 196,409 pounds
75. WASHINGTON, AL: 195,424 pounds
76. ALAMEDA, CA: 195,264 pounds
77. MERCER, PA: 193,328 pounds
78. CERRO GORDO, IA: 193,174 pounds
79. OTTAWA, MI: 192,420 pounds
80. DALLAS, TX: 191,695 pounds
81. HARVEY, KS: 187,711 pounds
82. PRICE, WI: 187,246 pounds
83. JEFFERSON, LA: 182,573 pounds
84. UNION, NJ: 182,463 pounds
85. CALDWELL, NC: 182,380 pounds
86. WOODFORD, KY: 181,281 pounds
87. HENRY, VA: 178,741 pounds
88. YORK, SC: 177,941 pounds
89. MCLEAN, IL: 177,258 pounds
90. BLACK HAWK, IA: 175,753 pounds
91. HENNEPIN, MN: 175,261 pounds

92. KING, WA: 169,326 pounds
93. ST. CHARLES, LA: 168,617 pounds
94. BRYAN, OK: 167,600 pounds
95. ROCK ISLAND, IL: 167,555 pounds
96. SMITH, TN: 166,365 pounds
97. JACKSON, MS: 162,109 pounds
98. AUGLAIZE, OH: 162,080 pounds
99. HARDY, WV: 161,586 pounds
100. LABETTE, KS: 158,034 pounds

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Zip Codes with Reported Total Environmental Releases

of XYLENE (MIXED ISOMERS) (1330-20-7) from the About The Chemicals section of Scorecard

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Ranked by (select your ranking criteria)

Total environmental releases

in

Entire United States Go (explain)

1. 30360 (GA): 1,259,910 pounds
2. 64119 (MO): 1,165,000 pounds
3. 49508 (MI): 903,210 pounds
4. 49423 (MI): 810,839 pounds
5. 76010 (TX): 779,000 pounds
6. 47905 (IN): 749,747 pounds
7. 66115 (KS): 731,047 pounds
8. 63042 (MO): 656,682 pounds
9. 48439 (MI): 629,457 pounds
10. 39701 (MS): 558,000 pounds
11. 43040 (OH): 509,100 pounds
12. 55371 (MN): 477,962 pounds
13. 46783 (IN): 473,000 pounds
14. 23523 (VA): 471,880 pounds
15. 08818 (NJ): 434,693 pounds
16. 40213 (KY): 430,270 pounds
17. 48341 (MI): 420,002 pounds
18. 73134 (OK): 418,300 pounds
19. 49512 (MI): 392,091 pounds
20. 48134 (MI): 376,998 pounds
21. 26062 (WV): 376,272 pounds
22. 76305 (TX): 375,007 pounds
23. 49631 (MI): 369,000 pounds
24. 40324 (KY): 365,469 pounds
25. 48184 (MI): 363,704 pounds

26. 55116 (MN): 363,000 pounds
27. 63385 (MO): 362,010 pounds
28. 44012 (OH): 359,000 pounds
29. 76801 (TX): 341,701 pounds
30. 48317 (MI): 334,000 pounds
31. 43610 (OH): 333,000 pounds
32. 30354 (GA): 331,700 pounds
33. 44481 (OH): 321,700 pounds
34. 37167 (TN): 318,487 pounds
35. 38063 (TN): 317,850 pounds
36. 48901 (MI): 315,000 pounds
37. 60633 (IL): 314,845 pounds
38. 77701 (TX): 314,668 pounds
39. 37172 (TN): 311,550 pounds
40. 21224 (MD): 302,390 pounds
41. 48160 (MI): 301,000 pounds
42. 68803 (NE): 300,000 pounds
43. 12150 (NY): 289,590 pounds
44. 77017 (TX): 281,995 pounds
45. 70601 (LA): 273,010 pounds
46. 53545 (WI): 272,000 pounds
47. 31709 (GA): 253,057 pounds
48. 48211 (MI): 250,750 pounds
49. 48121 (MI): 232,875 pounds
50. 37662 (TN): 230,610 pounds
51. 48359 (MI): 224,542 pounds
52. 19804 (DE): 221,282 pounds
53. 03874 (NH): 218,614 pounds
54. 64772 (MO): 213,300 pounds
55. 50208 (IA): 212,080 pounds
56. 45822 (OH): 210,871 pounds
57. 68127 (NE): 202,271 pounds
58. 23228 (VA): 201,866 pounds

59. 36553 (AL): 195,424 pounds
60. 50401 (IA): 193,174 pounds
61. 71129 (LA): 189,371 pounds
62. 61552 (IL): 188,394 pounds
63. 65708 (MO): 188,165 pounds
64. 97210 (OR): 187,969 pounds
65. 54555 (WI): 187,246 pounds
66. 35565 (AL): 186,827 pounds
67. 40241 (KY): 185,000 pounds
68. 40383 (KY): 181,281 pounds
69. 46368 (IN): 180,453 pounds
70. 29710 (SC): 177,695 pounds
71. 61761 (IL): 177,258 pounds
72. 78410 (TX): 163,742 pounds
73. 45885 (OH): 162,080 pounds
74. 26836 (WV): 161,586 pounds
75. 48091 (MI): 161,300 pounds
76. 67357 (KS): 158,034 pounds
77. 94538 (CA): 154,191 pounds
78. 43319 (OH): 153,000 pounds
79. 07036 (NJ): 152,211 pounds
80. 28633 (NC): 152,041 pounds
81. 32412 (FL): 151,240 pounds
82. 43607 (OH): 150,419 pounds
83. 50703 (IA): 149,876 pounds
84. 35207 (AL): 149,265 pounds
85. 71730 (AR): 147,822 pounds
86. 16125 (PA): 147,680 pounds
87. 63026 (MO): 145,600 pounds
88. 32401 (FL): 144,128 pounds
89. 70805 (LA): 143,169 pounds
90. 72908 (AR): 140,750 pounds
91. 55068 (MN): 140,492 pounds

92. 38802 (MS): 138,923 pounds
93. 35055 (AL): 136,349 pounds
94. 61244 (IL): 135,358 pounds
95. 53216 (WI): 133,750 pounds
96. 74820 (OK): 132,064 pounds
97. 87347 (NM): 130,416 pounds
98. 38901 (MS): 130,123 pounds
99. 35563 (AL): 129,072 pounds
100. 79110 (TX): 129,000 pounds

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Facilities with Reported Total Environmental Releases

of XYLENE (MIXED ISOMERS) (1330-20-7) from the About the Chemicals section of Scorecard

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Ranked by (select your ranking criteria)

Total environmental releases
in
Entire United States
from
All reporting sectors
Go (explain)

1. GM MLCG - DORAVILLE ASSEMBLY, DORAVILLE, GA: 1,258,000 Pounds
2. FORD MOTOR CO., KANSAS CITY ASSEMBLY PLANT, CLAYCOMO, MO: 1,165,000 Pounds
3. STEELCASE INC., GRAND RAPIDS, MI: 820,000 Pounds
4. AFCO INDS. INC., HOLLAND, MI: 773,000 Pounds
5. GMC TRUCK GROUP ARLINGTON ASSEMBLY PLANT, ARLINGTON, TX: 750,000 Pounds
6. GM MLCG-FAIRFAX ASSEMBLY, KANSAS CITY, KS: 690,250 Pounds
7. FORD MOTOR CO. ST. LOUIS ASSEMBLY, HAZELWOOD, MO: 652,000 Pounds
8. VEMCO INC., GRAND BLANC, MI: 629,457 Pounds
9. SUBARU-ISUZU AUTOMOTIVE INC., LAFAYETTE, IN: 565,600 Pounds
10. SANDERSON PLUMBING PRODS. INC., COLUMBUS, MS: 558,000 Pounds
11. HONDA OF AMERICA MFG. INC., MARYSVILLE, OH: 500,000 Pounds
12. GMTG FORT WAYNE ASSEMBLY, FORT WAYNE, IN: 473,000 Pounds
13. CRYSTAL CABINET WORKS INC., PRINCETON, MN: 464,258 Pounds
14. FORD MOTOR CO., LOUISVILLE ASSEMBLY PLANT, LOUISVILLE, KY: 430,270 Pounds
15. FORD EDISON ASSEMBLY PLANT, EDISON, NJ: 430,000 Pounds
16. GM SCG, OKLAHOMA CITY ASSEMBLY, OKLAHOMA CITY, OK: 418,300 Pounds
17. GENERAL MOTORS TRUCK GROUP PONTIAC E. ASSEMBLY, PONTIAC, MI: 411,000 Pounds
18. FORD MOTOR CO. NORFOLK ASSEMBLY PLANT, NORFOLK, VA: 398,000 Pounds

19. AUTOALLIANCE INTL. INC., FLAT ROCK, MI: 376,998 Pounds
20. TEXAS RECREATION CORP., WICHITA FALLS, TX: 375,007 Pounds
21. TEXTRON AUTOMOTIVE CO. - EVART PLANT, EVART, MI: 369,000 Pounds
22. TOYOTA MOTOR MFG. KENTUCKY INC., GEORGETOWN, KY: 365,455 Pounds
23. FORD MOTOR CO. - TWIN CITIES ASSEMBLY PLANT, SAINT PAUL, MN: 363,000 Pounds
24. GMTG WENTZILLE TRUCK ASSEMBLY, WENTZVILLE, MO: 362,000 Pounds
25. FORD MOTOR CO. OHIO ASSEMBLY PLANT, AVON LAKE, OH: 359,000 Pounds
26. 3M CO., BROWNWOOD, TX: 341,701 Pounds
27. FORD MOTOR CO. UTICA PLANT, SHELBY TOWNSHIP, MI: 334,000 Pounds
28. TOLEDO ASSEMBLY PLANT I, TOLEDO, OH: 333,000 Pounds
29. FORD MOTOR CO. ATLANTA ASSEMBLY PLANT, HAPEVILLE, GA: 331,700 Pounds
30. GM SCG LORDSTOWN ASSEMBLY, LORDSTOWN, OH: 321,000 Pounds
31. NISSAN MOTOR MFG. CORP. USA, SMYRNA, TN: 318,487 Pounds
32. GM LANSING PLANTS 2 3 & 6 (BODY), LANSING, MI: 315,000 Pounds
33. FORD MOTOR CO., CHICAGO ASSEMBLY PLANT, CHICAGO, IL: 310,680 Pounds
34. FORD MOTOR CO., MILAN PLASTICS PLANT, MILAN, MI: 301,000 Pounds
35. GMC NORTH AMERICAN TRUCK GROUP, BALTIMORE, MD: 300,360 Pounds
36. NEW HOLLAND N.A. INC., GRAND ISLAND, NE: 300,000 Pounds
37. SCHENECTADY INTL. INC., ROTTERDAM JUNCTION, NY: 289,590 Pounds
38. LYONDELL-CITGO REFINING CO. LTD., HOUSTON, TX: 281,787 Pounds
39. GMTG - JANESVILLE ASSEMBLY, JANESVILLE, WI: 272,000 Pounds
40. TEXTRON AUTOMOTIVE CO., AMERICUS, GA: 253,057 Pounds
41. GM MLCG - Hamtramck Assembly, DETROIT, MI: 250,750 Pounds
42. FORD MOTOR CO. DEARBORN ASSEMBLY PLANT, DEARBORN, MI: 232,000 Pounds
43. CITGO PETROLEUM CORP., LAKE CHARLES, LA: 231,550 Pounds
44. UNARCO MATERIAL HANDLING INC., SPRINGFIELD, TN: 231,513 Pounds
45. TENNESSEE EASTMAN DIV., KINGSPORT, TN: 230,610 Pounds
46. GMC NAO WILMINGTON ASSEMBLY PLANT, WILMINGTON, DE: 221,000 Pounds

47. VENTURE HOLDINGS CORP. BAILEY CORP., SEABROOK, NH: 215,430 Pounds
48. GM MCG - ORION ASSEMBLY, ORION, MI: 213,800 Pounds
49. 3M NEVADA PLANT, NEVADA, MO: 213,300 Pounds
50. MAYTAG APPLIANCES NLP 2, NEWTON, IA: 212,080 Pounds
51. HUFFY BICYCLE CO., CELINA, OH: 210,871 Pounds
52. QUEBECOR PRINTING RICHMOND INC., RICHMOND, VA: 201,366 Pounds
53. FORD MOTOR CO. - WAYNE ASSEMBLY PLANT, WAYNE, MI: 201,000 Pounds
54. STEELCASE WOOD FURNITURE, KENTWOOD, MI: 197,200 Pounds
55. CIBA SPECIALTY CHEMICALS CORP., MC INTOSH, AL: 195,424 Pounds
56. U.S. CAN CO. PLANT #20 WEIRTON, WEIRTON, WV: 195,293 Pounds
57. CATERPILLAR INC., MOSSVILLE COMPLEX, MOSSVILLE, IL: 188,394 Pounds
58. MOBIL OIL BEAUMONT REFY., BEAUMONT, TX: 188,000 Pounds
59. GEORGIA PACIFIC CORP., PHILLIPS, WI: 187,246 Pounds
60. GMTG - Shreveport Assembly, SHREVEPORT, LA: 186,500 Pounds
61. FORD MOTOR CO., KENTUCKY TRUCK PLANT, LOUISVILLE, KY: 185,000 Pounds
62. OSRAM SYLVANIA PRODS. INC., VERSAILLES, KY: 181,281 Pounds
63. SEQUA COATINGS CORP., PRECOAT METALS DIV., PORTAGE, IN: 180,453 Pounds
64. NORTH SAFETY PRODS., CLOVER, SC: 177,695 Pounds
65. MITSUBISHI MOTOR MFG. OF AMERICA INC., NORMAL, IL: 177,258 Pounds
66. GUNDERSON INC., PORTLAND, OR: 176,367 Pounds
67. KOCH REFINING CO. L.P., CORPUS CHRISTI, TX: 162,742 Pounds
68. FORD MOTOR CO., MICHIGAN TRUCK PLANT, WAYNE, MI: 162,700 Pounds
69. GOODYEAR TIRE & RUBBER CO., SAINT MARYS, OH: 162,080 Pounds
70. AMERICAN WOODMARK CORP., MOOREFIELD, WV: 161,586 Pounds
71. CHRYSLER CORP., WARREN TRUCK ASSEMBLY PLANT 1, WARREN, MI: 160,000 Pounds
72. HONDA OF AMERICA MFG. INC., EAST LIBERTY, OH: 153,000 Pounds
73. EB PIPE COATING INC., PANAMA CITY, FL: 151,240 Pounds
74. ABT BUILDING PRODS. A LOUISIANA-PACIFIC CO., TOLEDO, OH: 150,250 Pounds

75. EFCO CORP., MONETT, MO: 149,165 Pounds
76. A. O. SMITH ENGINEERED STORAGE PRODS. CO. (BOLTED), PARSONS, KS: 145,000 Pounds
77. ARIZONA CHEMICAL CO., PANAMA CITY, FL: 144,128 Pounds
78. NEW UNITED MOTOR MFG. INC., FREMONT, CA: 144,100 Pounds
79. WHIRLPOOL CORP., FORT SMITH, AR: 140,750 Pounds
80. WABASH NATL. CORP. MAIN PLANT, LAFAYETTE, IN: 138,750 Pounds
81. TOWER AUTOMOTIVE PRODS. CO., MILWAUKEE, WI: 133,750 Pounds
82. CAMROSE TECH. NOLOGIES L.L.C., ADA, OK: 132,064 Pounds
83. GIANT REFINING CO., JAMESTOWN, NM: 130,416 Pounds
84. HEATCRAFT INC., GRENADA, MS: 130,123 Pounds
85. 3M, GUIN, AL: 129,072 Pounds
86. OWENS-CORNING, AMARILLO, TX: 129,000 Pounds
87. THRALL CAR MFG. CO., CARTERSVILLE, GA: 127,510 Pounds
88. MAGNETEK RIPLEY, RIPLEY, TN: 125,550 Pounds
89. TENNESSEE ELECTROPLATING, RIPLEY, TN: 124,250 Pounds
90. TRINITY INDS. INC. PLT # 118, BEAUMONT, TX: 123,624 Pounds
91. HOVENSA L.L.C., CHRISTIANSTED, VI: 120,410 Pounds
92. VENTURE GRAND RAPIDS LLC, GRAND RAPIDS, MI: 120,327 Pounds
93. CHEM-FAB CORP., HOT SPRINGS, AR: 120,045 Pounds
94. HAY & FORAGE IND., HESSTON, KS: 120,000 Pounds
95. STATE INDS. INC., ASHLAND CITY, TN: 118,784 Pounds
96. STANDARD PRODS. CO., GRIFFIN, GA: 117,500 Pounds
97. GREAT DANE TRAILERS, SAVANNAH, GA: 117,461 Pounds
98. GM NAO FLINT OPS., FLINT, MI: 115,000 Pounds
99. CROWN CORK & SEAL CO. INC., SALISBURY, MD: 113,651 Pounds
100. FONTAINE TRAILER CO., HALEYVILLE, AL: 111,000 Pounds

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Industrial Sectors with Reported Total Environmental Releases

of XYLENE (MIXED ISOMERS) (1330-20-7) by Industrial Sector (2-digit SIC) from the About the Chemicals section of Scorecard

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Ranked by (select your ranking criteria)

Total environmental releases

in

Entire United States Go (explain)

1. 37: Transportation Equipment : 24,260,734 pounds
2. 34: Fabricated Metal Products : 8,482,120 pounds
3. 28: Chemicals And Allied Products : 5,078,886 pounds
4. 24: Lumber And Wood Products : 5,075,056 pounds
5. 25: Furniture And Fixtures : 4,725,061 pounds
6. 35: Industrial Machinery And Equipment : 4,520,579 pounds
7. 29: Petroleum And Coal Products : 4,139,749 pounds
8. 30: Rubber And Misc. Plastics Products : 3,424,050 pounds
9. 33: Primary Metal Industries : 2,366,144 pounds
10. 36: Electronic & Other Electric Equipment : 2,304,622 pounds
11. 39: Miscellaneous Manufacturing Industries : 961,899 pounds
12. 27: Printing And Publishing : 748,720 pounds
13. 32: Stone, Clay, And Glass Products : 688,705 pounds
14. 51: Wholesale Trade--Nondurable Goods : 465,545 pounds
15. 26: Paper And Allied Products : 360,488 pounds
16. 22: Textile Mill Products : 190,530 pounds
17. NA: Not reported : 181,621 pounds
18. 49: Electric, Gas, And Sanitary Services : 151,872 pounds
19. 38: Instruments And Related Products : 135,542 pounds
20. 17: Special Trade Contractors : 111,970 pounds
21. 97: National Security And Intl. Affairs : 82,364 pounds
22. 23: Apparel And Other Textile Products : 66,547 pounds
23. 20: Food And Kindred Products : 55,535 pounds
24. 73: Business Services : 25,739 pounds

25. 76: Miscellaneous Repair Services : 20,308 pounds
26. 31: Leather And Leather Products : 17,900 pounds
27. 13: Oil And Gas Extraction : 12,959 pounds
28. 67: Holding And Other Investment Offices : 11,667 pounds
29. 44: Water Transportation : 951 pounds
30. 87: Engineering & Management Services : 560 pounds
31. 95: Environmental Quality And Housing : 5 pounds

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Regulatory Coverage

of XYLENE (MIXED ISOMERS) (1330-20-7) from Scorecard

Federal Regulatory Program Lists

- Air Contaminants (Occupational and Safety Health Act)
- Hazardous Air Pollutants (Clean Air Act)
- Hazardous Substances (Superfund)
- Maximum Contaminant Levels (Safe Drinking Water Act)
- Registered Pesticides (Federal Insecticide, Fungicide, and Rodenticide Act)
- Toxic Release Inventory Chemicals

California State Regulatory Program Lists

- California Air Toxics "Hot Spots" Chemicals (Assembly Bill 2588)
- California Toxic Air Contaminants (Assembly Bill 1807)
- Maximum Contaminant Levels (California Safe Drinking Water Act)

Environmental Hazard Lists

- Dangerous for the Environment (Nordic Council of Ministers)

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Basic Testing to Identify Chemical Hazards

for XYLENE (MIXED ISOMERS) (1330-20-7) from Scorecard

The U.S. EPA conducted a comprehensive review of publicly available chemical testing data in 1997 to examine whether the basic information needed to identify chemical hazards is available for high production volume chemicals. EPA searched major chemical databases to determine if the following tests had been conducted on a chemical:

- Acute toxicity
- Chronic toxicity
- Neurotoxicity
- Developmental or reproductive toxicity
- Mutagenicity
- Carcinogenicity
- Ecotoxicity
- Environmental fate

Eight basic tests to identify chemical hazards have been conducted and are publicly available for this chemical.

More on the importance of basic toxicity testing

Reference

EPA. Chemical Hazard Data Availability Study: High Production Volume (HPV) Chemicals and SIDS Testing
Office of Pollution Prevention and Toxics, EPA,Washington, DC. 1998.

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Safety Assessment Data

for XYLENE (MIXED ISOMERS) (1330-20-7) from Scorecard

Are Risk Assessment Values Available?

Health Risk of Concern	Inhalation	Ingestion
Cancer	Not a recognized carcinogen	Not a recognized carcinogen
Noncancer	**No**	Yes

Are Exposure Data Available?

Type of Exposure	
Inhalation - ambient air	Monitoring data available in some states
Inhalation - indoor air	Yes
Ingestion	Yes

- See the data US EPA possesses for safety assessment.

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Scorecard Risk Characterization Data

for XYLENE (MIXED ISOMERS) (1330-20-7) from Scorecard

Risk Assessment Values or Standards

	Value	Units	Reference
Inhalation cancer risk value (potency)	Not a recognized or suspect carcinogen		
Inhalation noncancer risk value (reference concentration)	700	ug/m3	OEHHA2000-REL
National ambient air quality standard	Gap in regulatory coverage		
Ingestion cancer risk value (potency)	Not a recognized or suspect carcinogen		
Ingestion noncancer risk value (reference dose)	2	mg/kg-day	IRIS-HEAST
National water quality standard	10	mg/L	SDWA-MCL

See the data US EPA possesses for safety assessment.

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Chemical Classes

for XYLENE (MIXED ISOMERS) (1330-20-7) from Scorecard

Note that XYLENE (MIXED ISOMERS) may include any of the following constituents:

- M-XYLENE
- O-XYLENE
- P-XYLENE

Note that XYLENE (MIXED ISOMERS) may be a member of the following classes:

- VOLATILE ORGANIC COMPOUNDS

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Agency for Toxic Substances and Disease Registry

Public Health Statement

Xylene

ATSDR Public Health Statement, December 1990

This Statement was prepared to give you information about xylene and to emphasize the human health effects that may result from exposure to it. The Environmental Protection Agency (EPA) has identified 1,177 sites on its National Priorities List (NPL). Xylene has been found at 236 of these sites. However, we do not know how many of the 1,177 NPL sites have been evaluated for xylene. As EPA evaluates more sites, the number of sites at which xylene is found may change. The information is important for you because xylene may cause harmful health effects and because these sites are potential or actual sources of human exposure to xylene.

When a chemical is released from a large area such as an industrial plant, or from a container, such as a drum or bottle, it enters the environment as a chemical emission. This emission, which is also called a release, does not always lead to exposure. You can be exposed to a chemical only when you come into contact with the chemical. You may be exposed to it in the environment by breathing, eating, or drinking substances containing the chemical or from skin contact with it.

If you are exposed to a hazardous substance such as xylene, several factors will determine whether harmful health effects will occur and what the type and severity of those health effects will be. These factors include the dose (how much), the duration (how long), the route or pathway by which you are exposed (breathing, eating, drinking, or skin contact), the other chemicals to which you are exposed, and your individual characteristics such as age, sex, nutritional status, family traits, life style, and state of health.

What is xylene?

Xylene is primarily a man-made chemical. Chemical industries produce xylene from petroleum and to a smaller extent from coal. Xylene also occurs naturally in petroleum and coal tar, and is formed during forest fires. It is a colorless liquid with a sweet odor. There are three forms of xylene called isomers: *meta*-xylene, *ortho*-xylene, and *para*-xylene (*m*-, *o*- and *p*-xylene). Mixed xylene is a mixture of the three forms of xylene and smaller amounts of other chemicals, primarily ethylbenzene. Mixed xylene usually contains 6%-15% ethylbenzene, although it may contain higher amounts. The term "total xylenes," as

used in the title of this report, refers to the three forms or isomers of xylene (*meta-*, *ortho-* , and *para*-xylene) and also to mixed xylene. In this public health statement, the term "total xylenes" and xylene will be used interchangeably.

Solvents (liquids that can dissolve solids) and thinners for paints and varnishes often contain xylene, along with other solvents. Xylene is used as a solvent in the printing, rubber, and leather industries, and as a cleaning agent. It is also found in airplane fuel and gasoline, and is used as a material in the chemical, plastic, and synthetic fiber industries, and as an ingredient in the coating of fabrics and papers. Isomers of xylene are used in the manufacture of certain polymers, such as plastics.

Xylene evaporates and burns easily. Xylene does not mix well with water; however, it does mix with alcohol and with many other chemicals. Xylene is a liquid, and it can leak into soil, surface water (creeks, streams, rivers), or groundwater, where it may remain for 6 months or longer before it is broken down into other chemicals. However, because it evaporates readily, most xylene goes into the air, where it lasts for several days. During these several days in the air, the xylene is broken down by sunlight into other kinds of chemicals.

How might I be exposed to xylene?

You may become exposed to xylene because of its wide distribution in the environment. Releases of xylene occur primarily from industrial sources, automobile exhaust, and from the use of xylene as a solvent. Hazardous waste disposal sites and spills of xylene into the environment also serve as possible sources of exposure. Levels of xylene measured in industrial areas and cities of the United States and Europe range between 0.0007 and 0.09 parts of xylene per million parts of air (ppm). Xylene is sometimes released into water and soil as a result of the use, storage, and transport of petroleum products. Surface water generally contains less than 1 part of xylene per billion parts of water (ppb), although the level may be higher in industrial areas. Levels of xylene in public drinking water supplies range from 0 to 750 ppb. Because xylene evaporates rapidly, the presence of xylene in upper layers of soil is probably not large. Little information exists about the amount of xylene in food. Levels ranging between 0.05 ppm and 0.12 ppm xylene have been found in fish.

You may also come in contact with xylene from a variety of consumer products, including cigarette smoke, gasoline, paint, varnish, shellac, and rust preventives. Breathing vapors from these types of products can expose you to xylene. Indoor levels of xylene can be higher than outdoor levels, especially in buildings with poor ventilation. Skin contact with products containing xylene, such as solvents, lacquers, paint thinners and removers, and pesticides may also expose you to xylene.

In addition to painters (or paint industry workers), biomedical laboratory workers, distillers of xylene, wood processing plant workers, garage workers, metal workers, and furniture refinishers also may be exposed to xylene. Exposure to high levels of xylene is most likely to occur in workers who smoke and routinely come in contact with solvent products.

How can xylene enter and leave my body?

Xylene is most likely to enter your body through breathing xylene vapors. Less often, xylene enters the body through the skin following direct contact. Exposure to xylene may also take place by eating or drinking xylene- contaminated food or water. Xylene is rapidly absorbed by the lungs following breathing air containing xylene. The amount of xylene retained by the lungs ranges from 50% to 75% of the amount of xylene to which you are exposed. Physical exercise increases the amount of xylene absorbed by the lungs. Absorption of xylene after eating food or drinking water containing it is both rapid and complete. Absorption of xylene through the skin also occurs rapidly following direct contact with xylene or exposure to xylene vapors in the air. At hazardous waste sites, breathing xylene vapors, drinking wellwater contaminated with xylene, and direct contact of the skin with xylene are possible ways you can be exposed. Xylene passes into the blood soon after entering the body.

In humans and laboratory animals, xylene is broken down into other chemicals in the liver and lungs. This process changes most of the xylene that is breathed in or swallowed into a different form. Once xylene has been broken down, the breakdown products rapidly leave the body, mainly in urine but some unchanged xylene also leaves in breath from the lungs. Small amounts of broken down xylene have appeared in urine of humans as soon as 2 hours after breathing air containing xylene. Usually most of the xylene that is taken in leaves the body within 18 hours after exposure ends. Storage of xylene in fat or muscle may prolong the time needed for xylene to leave the body.

How can xylene affect my health?

Short-term exposure of humans to high levels of xylene or chemical mixtures containing xylene causes irritation of the skin, eyes, nose, and throat; difficulty in breathing; impaired function of the lungs; delayed response to a visual stimulus; impaired memory; stomach discomfort; and possible changes in the liver and kidneys. Death can occur in individuals who are exposed to very high levels of xylene for a short period of time. Both short- and long-term exposure to high concentrations of xylene can also cause a number of effects on the nervous system, such as headaches, lack of muscle coordination, dizziness, confusion, and changes in one's sense of balance.

Results of studies with animals indicate that large amounts of xylene can cause changes in the liver and adverse effects on the kidney, lung, heart, and nervous system. Short-term exposure to high concentrations of xylene causes death in some animals, as well as muscular spasms, incoordination, hearing loss, changes in behavior, changes in organ weights, and changes in enzyme activity. Long-term exposure to low concentrations of xylene has not been well studied in animals.

Information from animal studies is not adequate to determine whether or not xylene causes cancer in humans. The International Agency for Research on Cancer has determined that xylene is not classifiable as to its carcinogenicity to humans. However, exposure of pregnant women to high levels of xylene may cause adverse effects in the fetus. Studies with unborn animals indicate that high levels of xylene may cause increased numbers of deaths, decreased weight, skeletal changes, and delayed skeletal development. In many instances, the levels of xylenes causing these effects also caused the mothers to be ill. The higher the level of exposure and the longer the exposure to xylene, the greater the chance for adverse health effects.

What levels of exposure have resulted in harmful health effects?

Xylene or chemical mixtures containing xylene are deadly to humans if large enough quantities are swallowed or inhaled. However, the levels which cause death in humans are not known. Lower levels (100-299 ppm) of inhaled xylene can cause eye, nose, and throat irritation, delayed response to a visual stimulus, and poor memory. Direct contact of humans with several drops of xylene causes skin irritation. The lowest level at which you can detect the odor of xylene in air ranges from 0.1 ppm to 2.0 ppm.

In animals, moderate to high levels (1,300-2,000 ppm) of xylene inhaled for short periods of time may cause decreased breathing rate, hearing loss, inactivity, unconsciousness, and biochemical changes in the brain. With longer-term inhalation, adverse health effects in animals generally occur at lower levels (230-800 ppm). In animals breathing high levels of xylene over long-term exposures, possible adverse health effects include changes in heart rate and blood flow, changes in the chemical composition of nerves, and hearing loss. In animals given high levels (5,000 ppm) of xylene orally over short-term exposures, a possible adverse health effect is impaired eye function. In animals exposed by mouth to very high levels (40,000 ppm) of xylene, death can occur.

Tables 1-1, 1-2, 1-3, and 1-4 show the relationship between exposure to xylene and known health effects.

Is there a medical test to determine whether I have been exposed to xylene?

Medical tests are available to determine if you have been exposed to xylene at greater than normal background levels. Confirmation of xylene exposure is determined by measuring xylene's breakdown products that are eliminated from the body in the urine. These urinary measurements will specifically determine if you have been exposed to xylene. There is a high degree of agreement between exposure to xylene and the levels of xylene's breakdown products in the urine. A urine sample must be provided soon after exposure ends, because xylene quickly leaves the body. Alcohol and aspirin may affect the test results. Available tests can only indicate exposure to xylene; they cannot be used to predict which health effects, if any, will develop.

What recommendations has the federal government made to protect human health?

The U.S. Environmental Protection Agency (EPA) estimates that for an adult of average weight, exposure to 0.4 milligrams of xylene per liter (mg/L or ppm) of water each day for a lifetime (70 years) is unlikely to result in noncancerous adverse health effects. For a long-term, but less than lifetime, exposure (about 7 years), 27.3 ppm is estimated to be a level unlikely to result in noncancerous adverse health effects for an adult. Exposure to 12 ppm of xylene in water for 1 day or to 7.8 ppm of xylene in water for 10 days or longer is unlikely to present a noncancerous health risk to a small child. EPA has proposed a recommended maximum level of 0.44 ppm for xylene in drinking water.

To protect individuals from the potential adverse health effects of xylene, the federal government regulates xylene in the environment. The Occupational Safety and Health Administration (OSHA) has set up a legally enforceable occupational exposure limit of 100 ppm of xylene in air averaged over an 8-hour workday, and a 15- minute exposure limit of 150 ppm. The National Institute for Occupational Safety and Health (NIOSH) has recommended an exposure limit of 100 ppm of xylene averaged over a workday up to 10 hours long in a 40-hour workweek. NIOSH has also recommended that exposure to xylene not exceed 200 ppm for longer than 15 minutes. NIOSH has classified xylene exposures of 10,000 ppm as immediately dangerous to life or health.

EPA and the Food and Drug Administration (FDA) specify conditions under which xylene may be used as a part of herbicides, pesticides, or articles that are used in contact with food.

EPA reportable quantity regulations require that a spill of 1,000 pounds or more of xylene or used xylene solvents be reported to the Federal Government National Response Center.

Where can I get more information?

If you have any more questions or concerns not covered here, please contact your state health or environmental department or:

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Agency for Toxic Substances and Disease Registry
Division of Toxicology
1600 Clifton Road, E-29
Atlanta, Georgia 30333
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This agency can also give you information on the location of the nearest occupational and environmental health clinics. Such clinics specialize in recognizing, evaluating, and treating illnesses that result from exposure to hazardous substances.

ToxFAQs

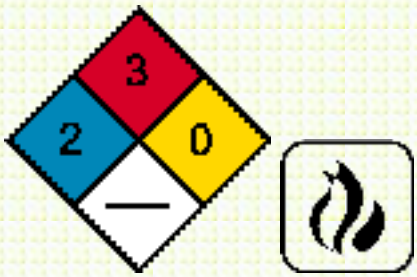
Xylene

CAS# 1330-20-7

September 1996

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p-Xylene
C_8H_{10}
Stereo Image
XYZ File



NFPA Label Key

Material Safety Data Sheet
(University of Utah)

Agency for Toxic Substances and Disease Registry

This fact sheet answers the most frequently asked health questions about xylene. For more information, you may call the ATSDR Information Center at 1-800-447-1544. This fact sheet is one in a series of summaries about hazardous substances and their health effects. The effects of exposure to any hazardous substance depend on the dose, the duration, how you are exposed, personal traits and habits, and whether other chemicals are present. It's important you understand this information because this substance may harm you; refer to the glossary for definitions of any technical words.

SUMMARY: Exposure to xylene occurs in the workplace and when you use paint, gasoline, paint thinners and other products that contain it. People who breathe high levels may have dizziness, confusion, and a change in their sense of balance. This substance has been found in at least 658 of the 1,430 National Priorities List sites identified by the Environmental Protection Agency (EPA).

What is xylene?
(Pronounced zy'leen)

Xylene is a colorless, sweet-smelling liquid that catches on fire easily. It occurs naturally in petroleum

and coal tar and is formed during forest fires. You can smell xylene in air at 0.08-3.7 parts of xylene per million parts of air (ppm) and begin to taste it in water at 0.53-1.8 ppm.

Chemical industries produce xylene from petroleum. It's one of the top 30 chemicals produced in the United States in terms of volume.

Xylene is used as a solvent and in the printing, rubber, and leather industries. It is also used as a cleaning agent, a thinner for paint, and in paints and varnishes. It is found in small amounts in airplane fuel and gasoline.

What happens to xylene when it enters the environment?

- Xylene has been found in waste sites and landfills when discarded as used solvent, or in varnish, paint, or paint thinners.
- It evaporates quickly from the soil and surface water into the air.
- In the air, it is broken down by sunlight into other less harmful chemicals.
- It is broken down by microorganisms in soil and water.
- Only a small amount of it builds up in fish, shellfish, plants, and animals living in xylene-contaminated water.

How might I be exposed to xylene?

- Breathing xylene in workplace air or in automobile exhaust.
- Breathing contaminated air.
- Touching gasoline, paint, paint removers, varnish, shellac, and rust preventatives that contain it.
- Breathing cigarette smoke that has small amounts of xylene in it.
- Drinking contaminated water or breathing air near waste sites and landfills that contain xylene.
- The amount of xylene in food is likely to be low.

How can xylene affect my health?

Xylene affects the brain. High levels from exposure for **short periods** (14 days or less) or **long periods** (more than 1 year) can cause headaches, lack of muscle coordination, dizziness, confusion, and changes in one's sense of balance. Exposure of people to **high levels** of xylene for **short periods** can also cause irritation of the skin, eyes, nose, and throat; difficulty in breathing; problems with the lungs; delayed reaction time; memory difficulties; stomach discomfort; and possibly changes in the liver and kidneys. It can cause unconsciousness and even death at **very high levels**.

Studies of unborn animals indicate that **high concentrations** of xylene may cause increased numbers of deaths, and delayed growth and development. In many instances, these same concentrations also cause damage to the mothers. We do not know if xylene harms the unborn child if the mother is exposed to **low levels** of xylene during pregnancy.

How likely is xylene to cause cancer?

The **International Agency for Research on Cancer (IARC)** has determined that xylene is not classifiable as to its carcinogenicity in humans.

Human and animal studies have not shown xylene to be carcinogenic, but these studies are not

conclusive and do not provide enough information to conclude that xylene does not cause cancer.

Is there a medical test to show whether I've been exposed to xylene?

Laboratory tests can detect xylene or its breakdown products in exhaled air, blood, or urine. There is a high degree of agreement between the levels of exposure to xylene and the levels of xylene breakdown products in the urine. However, a urine sample must be provided very soon after exposure ends because xylene quickly leaves the body. These tests are not routinely available at your doctor's office.

Has the federal government made recommendations to protect human health?

The **EPA** has set a limit of 10 ppm of xylene in drinking water.

The **EPA** requires that spills or accidental releases of xylenes into the environment of 1,000 pounds or more must be reported.

The **Occupational Safety and Health Administration (OSHA)** has set a maximum level of 100 ppm xylene in workplace air for an 8-hour workday, 40-hour workweek.

The **National Institute for Occupational Safety and Health (NIOSH)** and the **American Conference of Governmental Industrial Hygienists (ACGIH)** also recommend exposure limits of 100 ppm in workplace air.

NIOSH has recommended that 900 ppm of xylene be considered immediately dangerous to life or health. This is the exposure level of a chemical that is likely to cause permanent health problems or death.

Glossary

Evaporate:

To change from a liquid into a vapor or a gas.

Carcinogenic:

Having the ability to cause cancer.

CAS:

Chemical Abstract Service.

PPM:

Parts per million.

Solvent:

A liquid that can dissolve other substances.

References

Agency for Toxic Substances and Disease Registry (ATSDR). 1995. Toxicological profile for xylenes (Update). Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service.

Where can I get more information?

ATSDR can tell you where to find occupational and environmental health clinics. Their specialists can recognize, evaluate, and treat illnesses resulting from exposure to hazardous substances. You can also contact your community or state health or environmental quality department if you have any more

questions or concerns.

For more information, contact:

Agency for Toxic Substances and Disease Registry
Division of Toxicology
1600 Clifton Road NE, Mailstop E-29
Atlanta, GA 30333
Phone: 1-800-447-1544
Fax: 404-639-6359



U.S. Department of Health and Human Services
Public Health Service
Agency for Toxic Substances and Disease Registry

Link to ToxFAQs Home Page

Link to ATSDR Science Corner

Link to ATSDR Home Page

XYLENES (Isomers and Mixture)

Xylenes (isomers and mixture) are federal hazardous air pollutants and were identified as toxic air contaminants in April 1993 under AB 2728.

Molecular Formula: C_8H_{10}

This fact sheet refers to the mixture of m-xylene, o-xylene, and p-xylene (mixed xylenes). Mixed xylenes are colorless liquids that are insoluble in water and miscible with alcohol, ether, and many other organic solvents. The commercial mixed xylenes are composed of the three isomers, with the m- and p- isomers predominating. For particular purposes, the m-, o-, or p- isomer may be separated. They are insoluble in water (HSDB, 1991; Sax, 1987).

Physical Properties of Mixed Xylenes

	m-Xylene	o-Xylene	p-Xylene
CAS Registry Number	108-38-3	95-47-6	106-42-3
Molecular Weight	106.18	106.18	106.18
Boiling Point	139.3 °C	144.4 °C	137-138 °C
Melting Point	-47.4 °C	-25.2 °C	13-14 °C
Flash Point	77 °F (closed cup)	62.6 °F	77 °F (closed cup)
Vapor Density	3.66 (air = 1)		3.66 (air=1)
Vapor Pressure	8.3 mm Hg at 25 °C	6.6 mm Hg at 25 °C	8.7 mm Hg at 25 °C
Density/Specific Gravity	0.8684 at 15/4 °C water=1	0.880 at 20/4 °C water=1	0.86104 at 20/4 °C water=1
Log Octanol/WaterPartition Coefficient:	3.20	3.12	3.15
Conversion Factor:	1 ppm = 4.3 mg/m^3	1 ppm = 4.3 mg/m^3	1 ppm = 4.3 mg/m^3

(Howard, 1990; Merck, 1989; Sax, 1987; Sax, 1989)

SOURCES AND EMISSIONS

A. Sources

Emissions of mixed xylenes have been detected from petroleum refining, motor vehicles, residential wood-burning stoves and fireplaces. Mixed xylenes are used as chemical intermediates, as solvents, in aviation fuel, and in household products such as aerosol paints and lacquers (Howard, 1990).

Xylene is registered as an insecticide. Only one product containing xylene is still registered, although use of this product has been suspended since 1993. It was registered for use on fruit, vegetable and grain crops, on ornamental lawns, gardens and plants. It may be applied to dogs, and animal dwellings as well

as around houses and farm buildings (DPR, 1996).

The licensing and regulation of pesticides for sale and use in California are the responsibility of the Department of Pesticide Regulation (DPR). Information presented in this fact sheet regarding the permitted pesticidal uses of xylene has been collected from pesticide labels registered for use in California and from DPR's pesticide databases. This information reflects pesticide use and permitted uses in California as of October 15, 1996. For further information regarding the pesticidal uses of this compound, please contact the Pesticide Registration Branch of DPR (DPR, 1996).

The primary stationary sources that have reported emissions of m-, o-, and p-xylene in California are manufacturers of motor vehicles and equipment, manufacturers of metal cans and shipping containers, and petroleum refining (ARB, 1997b).

B. Emissions

The total emissions of m-, o-, and p-xylene from stationary sources in California are estimated to be at least 30,000 pounds, 34,000 pounds, and 51,000 pounds per year, respectively, based on data reported under the Air Toxics "Hot Spots" Program (AB 2588). In addition, there are also approximately 4 million pounds of unspecified xylenes in addition to those listed individually (ARB, 1997b).

C. Natural Occurrence

m- and p-Xylene occur naturally in petroleum. o-Xylene is found in coal tar, petroleum, forest fires and plant volatiles (Howard, 1990).

AMBIENT CONCENTRATIONS

m-, o-, and p-Xylene are routinely monitored by the statewide Air Resources Board air toxics network. The network's mean concentration of m- and p-xylene from January 1996 through December 1996 is estimated to be 4.17 micrograms per cubic meter ($\mu g/m^3$) or 0.97 parts per billion (ppb). The network's mean concentration of o-xylene, from January 1996 through December 1996, is estimated to be 1.55 µg/m3 or 0.36 ppb (ARB, 1997c).

The United States Environmental Protection Agency (U.S. EPA) has also compiled ambient data from 31 study areas throughout the United States on p-xylene from 1985-87. The U.S. EPA reported an overall p-xylene mean concentration of 8.7 $\mu g/m^3$ or 2.0 ppb. The U.S. EPA has also compiled ambient o- and m-xylene data from three study areas throughout the United States from 1989-91. The U.S. EPA reported an overall o-xylene mean concentration of 2.6 $\mu g/m^3$ or 0.6 ppb and an overall m-xylene mean concentration of 5.4 $\mu g/m^3$ or 1.3 ppb (U.S. EPA, 1993a).

INDOOR SOURCES AND CONCENTRATIONS

m-, o-, and p-Xylene are widely used as solvents and are present in numerous consumer products. Consumer products with the highest median emissions of xylenes include pens/inks and coatings. Xylenes are also emitted from building materials such as carpet adhesives, vinyl cove adhesive, latex

caulk, latex paint, and various moldings. Environmental tobacco smoke is also a common indoor source of xylenes (Hodgson and Wooley, 1991).

Indoor residential concentrations of m-, p-, and o-xylene have been measured in several studies. The California Total Exposure Assessment Methodology (TEAM) studies were conducted in 1984 and 1987 in and around Los Angeles and Contra Costa County. Because of their physical similarities, m-xylene and p-xylene have been reported as a single value. The mean m- and p-xylene concentrations from these studies ranged from 9.3 to 33.6 µg/m^3. The mean o-xylene concentrations from these studies ranged from 3.71 to 12.9 µg/m^3. Indoor values from these studies were consistently higher than outdoor values. The indoor/outdoor ratio was approximately 1.5 to 2.5. (Pelizzari, 1987b; 1989).

In a residential study conducted in Woodland, California m-, p-, and o-xylene were quantifiable in 99 percent of the 125 samples. The indoor average m-, p-xylene concentration was 7.4 µg/m^3 and the values ranged from below the quantifiable level of 0.35 to 120 µg/m^3. The indoor average o-xylene concentration from that study was 3.3 µg/m^3 and the values ranged from below the quantifiable level of 0.1 to 49 µg/m^3. The indoor/outdoor ratio of m-, p-, and o-xylene in this study was 4.6 µg/m3 (Sheldon et al., 1992).

In-vehicle concentrations of m-, p-, and o-xylene were 2 to 6 times higher than outdoor levels. In southern California, a total xylene average concentration of 32.9 µg/m^3 and a maximum concentration of 254 µg/m^3 were measured (Shikiya et al., 1989). In Boston, an average m-, p-xylene of 20.9 µg/m^3 and a maximum of 74.6 µg/m^3 were recorded. The average and maximum concentrations of o-xylene during this study were 7.3 µg/m^3 and 26.1 µg/m^3, respectively (Chan et al., 1991b). Similar results were observed in a Raleigh, North Carolina in-vehicle study (Chan et al., 1991a).

Emissions of m-, p- Xylene averaged 299 µg/cigarette in environmental tobacco smoke in a chamber study of six brands of cigarettes popular in California (Daisey et al., 1994). Emissions of o-xylene averaged 67 µg/cigarette in environmental tobacco smoke.

ATMOSPHERIC PERSISTENCE

The atmospheric lifetime of m-xylene is 14 to 15 hours. The atmospheric lifetime of o-xylene is 25 to 26 hours. The atmospheric lifetime of p-xylene is 24 to 25 hours (Kao, 1994).

The reaction products of m-xylene are m-tolualdehyde, m-methyl benzyl nitrate, nitro-m-xylene, dimethylphenols, formaldehyde, glyoxal, and methyl glyoxal. The reaction products of o-xylene are o-tolualdehyde, o-methyl benzyl nitrate, nitro-o-xylene, dimethylphenols, formaldehyde, glyoxal, methyl glyoxal, and biacetyl. The reaction products of p-xylene are p-tolualdehyde, p-methyl benzyl nitrate, nitro-p-xylene, dimethylphenols, formaldehyde, glyoxal, and methyl glyoxal (Kao, 1994).

AB 2588 RISK ASSESSMENT INFORMATION

The Office of Environmental Health Hazard Assessment reviews risk assessments submitted under the Air Toxics "Hot Spots" Program. Of the risk assessments reviewed as of December 1996, for non-cancer health effects, xylenes contributed to the total hazard index in 46 of the approximately 89 risk

assessments reporting a total chronic hazard index greater than 1. Xylenes also contributed to the total hazard index in 42 of the approximately 107 risk assessments reporting a total acute hazard index greater than 1 (OEHHA, 1996b).

HEALTH EFFECTS

Probable routes of human exposure to xylenes are inhalation, ingestion, and dermal contact (U.S. EPA, 1994a).

Non-Cancer: Exposure to xylene vapors may cause eye, nose, throat, and respiratory tract irritation. Xylene is a central nervous system depressant. Acute exposure may cause gastrointestinal effects such as nausea, vomiting, and gastric irritation. By analogy to toluene and benzene, xylene is predicted to cause cardiac arrythmias. Exposure may injure the kidneys.

An acute non-cancer Reference Exposure Level (REL) of 4.4 x 10^3 µg/m^3 and a chronic non-cancer REL of 3 x 102 µg/m^3 are listed for mixed xylenes in the California Air Pollution Control Officers Association Air Toxics "Hot Spots" Program, Revised 1992 Risk Assessment Guidelines. The toxicological endpoint considered for acute toxicity is respiratory irritation. The toxicological endpoints considered for chronic toxicity are the respiratory system and reproductive system including teratogenic and developmental effects (CAPCOA, 1993). The U.S. EPA is currently reviewing the Reference Concentration (RfC) for mixed xylenes, m-, o-, and p-xylenes. The U.S. EPA has established an oral reference dose (RfD) of 2 milligrams per kilogram per day (mg/kg/d) for mixed xylenes based on hyperactivity, decreased body weight, and increased mortality in rats. The provisional RfD for m- and o-xylenes is also 2 mg/kg/d. The U.S. EPA estimates that consumption of this dose or less, over a lifetime, would not likely result in the occurrence of chronic, non-cancer effects. The U.S. EPA has not established an RfD for p-xylenes (U.S. EPA, 1994a).

In mice, rats, and rabbits, inhalation of mixed xylene or one of o-, m-, or p-xylene has resulted in increased post-implantation loss, reduced fetal weight, and other indications of retarded development. Oral exposure at high levels in mice has produced cleft palate and reduced fetal weight (ATSDR, 1993i; IARC, 1989c; HSDB, 1995).

Cancer: No information is available on the carcinogenic effects of mixed xylenes in humans. The U.S. EPA has classified xylene (isomers and mixtures) in Group D: Not classifiable as a carcinogen (U.S. EPA, 1994a). The International Agency for Research on Cancer has classified xylene (isomers and mixtures) in Group 3: Not classifiable as to carcinogenicity (IARC, 1987a).

XYLENES[(1)]

1330-20-7

Hazard Summary

CAUTION: Unless otherwise noted, the quantitative information on these fact sheets are from "EPA Health Effects Notebook for Hazardous Air Pollutants-Draft", EPA-452/D-95-00, PB95-503579, December 1994." Please conduct a current literature search and check the appropriate current online database for the most recent quantitative information.

- Acute (short-term) inhalation exposure to mixed xylenes in humans results in **irritation of the nose and throat, gastrointestinal effects such as nausea, vomiting, and gastric irritation, mild transient eye irritation, and neurological effects.**
- Chronic (long-term) inhalation exposure of humans to mixed xylenes results primarily in **central nervous system (CNS) effects, such as headache, dizziness, fatigue, tremors and incoordination.** Other effects noted include labored breathing and impaired pulmonary function, increased heart palpitation, severe chest pain and an abnormal EKG, and possible effects on the blood and kidney.
- The Reference Concentration (RfC) for mixed xylenes, *m*-, *o*-, and *p*-xylenes is under review by the U.S. Environmental Protection Agency (EPA).
- The Reference Dose (RfD) for mixed xylenes is 2 mg/kg/d.[a] The provisional RfD for *m*- and *o*-xylenes is also 2 mg/kg/d. EPA estimates that consumption of this dose or less, over a lifetime, would not likely result in the occurrence of chronic noncancer effects.[b]
- Insufficient data are available on the developmental or reproductive effects of mixed xylenes in humans. Animal studies have reported **developmental effects, such as an increased incidence of skeletal variations in fetuses, and fetal resorptions via inhalation.**
- No information is available on the carcinogenic effects of mixed xylenes in humans, and animal studies have reported negative results from exposure via gavage (experimentally placing the chemical in the stomach). EPA has classified mixed xylenes as a Group D, **not classifiable as to human carcinogenicity.**

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[a] Milligrams per kilogram per day is one way to measure the amount of the contaminant that is consumed

in food.

[b] The RfD is not a direct estimator of risk but rather a reference point to gauge the potential effects. Exceedance of the RfD does not imply that an adverse health effect would necessarily occur. As the amount and frequency of exposures exceeding the RfD increase, the probability of adverse health effects also increases. The provisional RfD is a value that has had some form of Agency review, but it does not appear on the IRIS system.

Please Note: The main sources of information for this fact sheet are EPA's Integrated Risk Information System (IRIS), which contains information on oral chronic toxicity and the RfD, and the Agency for Toxic Substances and Disease Registry's (ATSDR's) *Toxicological Profile for Xylenes*. Other secondary sources include the Hazardous Substances Data Bank (HSDB), a database of summaries of peer-reviewed literature, and the Registry of Toxic Effects of Chemical Substances (RTECS), a database of toxic effects that are not peer reviewed.

Environmental/Occupational Exposure

- Mixed xylenes are distributed throughout the environment; they have been detected in air, rainwater, soils, surface water, sediments, drinking water, and aquatic organisms. (1)
- Ambient air concentrations of mixed xylenes in urban areas of the United States range from 0.003 to 0.38 mg/m^3. (1)
- Mixed xylenes have also been detected in indoor air; xylenes have been widely used in home use products such as paints. One study reported concentrations of *m*- and *p*-xylene ranging from 0.010 to 0.047 mg/m^3. (1)
- Levels of mixed xylenes in drinking water have been reported to range from 0.2 to 9.9 g/L, with mean concentrations of less than 2 g/L. (1)
- Occupational exposure to mixed xylenes may occur at workplaces where mixed xylenes are produced and used as industrial solvents. (1)
- Xylene exposure may be to any of the three isomers or to mixtures of the isomers. (1)

Assessing Personal Exposure

- Exposure to mixed xylenes may be determined by measuring the breakdown products of mixed xylenes in the urine. (1)

Health Hazard Information

Acute Effects:

- Human and animal data show that all xylene isomers or xylene mixtures produce similar effects, although specific isomers may not be equally potent in producing the effects. (1)
- Acute (short-term) inhalation exposure to mixed xylenes in humans has been associated with dyspnea and irritation of the nose and throat; gastrointestinal effects such as nausea, vomiting, and gastric discomfort; mild transient eye irritation; and neurological effects such as impaired short-term memory, impaired reaction time, performance decrements in numerical ability, and alterations in equilibrium and body balance. Acute dermal exposure in humans results in transient skin irritation

and dryness and scaling of the skin. (1-3)

- Acute inhalation exposure to a mixture of toluene and xylenes resulted in more than additive respiratory and neurological toxicity. (1)
- Acute animal studies have reported effects on the respiratory, cardiovascular, and central nervous systems and the kidney from inhalation exposure to mixed xylenes. (1)
- Acute animal tests, such as the LC_{50} and LD_{50} tests in rats and mice, have shown mixed xylenes to have low to moderate toxicity from inhalation exposure and moderate toxicity from oral exposure. (4,5)

Chronic Effects (Noncancer):

- Chronic (long-term) exposure of humans to mixed xylenes, as seen in occupational settings, has resulted primarily in neurological effects such as headache, dizziness, fatigue, tremors, and incoordination. Labored breathing, impaired pulmonary function, increased heart palpitation, severe chest pain, an abnormal EKG, and possible effects on the blood and kidney have also been reported. (1,2)
- Mixed xylenes have not been extensively tested for chronic effects, although animal studies show effects on the liver from inhalation exposure and effects on the blood, kidney, and CNS from oral exposure to mixed xylenes. (1)
- The RfC for mixed xylenes, *m*-, *o*-, and *p*-xylenes is under review by EPA. (6-9)
- The RfD for mixed xylenes is 2 mg/kg/d based on hyperactivity, decreased body weight, and increased mortality in rats, and the provisional RfD for *m*- and *o*-xylenes is also 2 mg/kg/d. EPA has not established an RfD or a provisional RfD for *p*-xylenes. (6,10)
- EPA has medium confidence in the study on which the RfD was based because it was a well-designed study in which adequately sized groups of two species were tested over a substantial portion of their lifespan, comprehensive histology was performed, and a no-observed-adverse-effect level (NOAEL) was defined; but clinical chemistries, blood enzymes, and urinalysis were not performed; medium confidence in the database because even though supporting data exist for mice, and teratogenicity and fetotoxicity data are available with positive results at high oral doses, a lowest-observed-adverse-effect level (LOAEL) for chronic oral exposure has not been defined; and, consequently, medium confidence in the RfD. (6)
- EPA's Office of Air Quality Planning and Standards, for a hazard ranking under Section 112(g) of the Clean Air Act Amendments, has evaluated mixed xylenes for chronic toxicity and has given them a composite score of 8 (scores range from 1 to 100, with 100 being the most toxic). These scores are nonlinear and are the product of two ratings: a rating based on the minimal-effect-dose and a rating based on the type of effect. (11)

Reproductive/Developmental Effects:

- Several human studies examined exposure to organic solvents (including mixed xylenes) and developmental effects. However, no conclusions can be drawn from these studies because they all involved concurrent exposure to multiple chemicals. (1)
- Mixed xylenes have been shown to produce developmental effects, such as an increased incidence of skeletal variations in fetuses, delayed ossification, fetal resorptions, hemorrhages in fetal organs, and decreased fetal body weight in animals via inhalation exposure. Some studies observed maternal

toxicity as well. (1-3)

Cancer Risk:

- No information is available on the carcinogenic effects of mixed xylenes in humans. (1)
- An increase in tumors was not reported in an animal study of exposure to mixed xylenes via gavage (experimentally placing the chemical in the stomach). Other animal studies have reported equivocal results. (1,3)
- EPA has classified mixed xylenes as a Group D, not classifiable as to human carcinogenicity. (6)

Physical Properties

- Mixed xylenes are colorless liquids with a sweet odor. (1)
- The odor threshold for *m*-xylene is 1.1 ppm. (4)
- The chemical formula for mixed xylenes is C_8H_{10}, and the molecular weight is 106.16 g/mol. (1)
- The vapor pressure for mixed xylenes is 6.72 mm Hg at 21 C, and the octanol/water partition coefficient (Log K_{ow}) is 3.12-3.20. (1)

Uses

- Mixed xylenes are used in the production of ethylbenzene, in solvents, and for paints and coatings and are blended into gasoline. (1)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) × (molecular weight of the compound)/(24.45). For xylenes: 1 ppm = 4.34 mg/m^3.

Health Data from Inhalation Exposure

Concentration (mg/m^3)	Health numbers[a]	Regulatory, advisory numbers[b]	Reference
1,000,000.0			
-- -- -- -- 100,000.0			
-- -- -- -- 10,000.0	• LC_{50} (mixed xylenes) (27,571 mg/m^3) • LC_{50} (*p*-xylene) (16,963 mg/m^3)		1,5 1,5

-- -- -- -- 1,000.0			
-- -- -- -- 100.0		• NIOSH REL (ceiling) (868 mg/m^3) • OSHA PEL and ACGIH TLV (STEL) (655 mg/m^3) • OSHA PEL, ACGIH TLV, and NIOSH REL (435 mg/m^3)	2 2 2

ACGIH STEL--American Conference of Governmental and Industrial Hygienists' short-term exposure limit; 15-min time-weighted-average exposure that should not be exceeded at any time during a workday even if the 8-h time-weighted-average is within the threshold limit value.
ACGIH TLV--American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.
LC_{50} (Lethal Concentration$_{50}$)--A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.
NIOSH REL--National Institute of Occupational Safety and Health's recommended exposure limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling.
OSHA PEL--Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.

References

1. **Agency for Toxic Substances and Disease Registry (ATSDR). *Toxicological Profile for Xylenes*. U.S. Public Health Service, U.S. Department of Health and Human Services, Altanta, GA. 1993.**
2. **E.J. Calabrese and E.M. Kenyon. *Air Toxics and Risk Assessment*. Lewis Publishers, Chelsea, MI. 1991.**
3. **U.S. Department of Health and Human Services. Hazardous Substances Data Bank (HSDB, online database). National Toxicology Information Program, National Library of Medicine,**

Bethesda, MD. 1993.

4. **J.E. Amoore and E. Hautala. Odor as an aid to chemical safety: Odor thresholds compared with threshold limit values and volatilities for 214 industrial chemicals in air and water dilution. *Journal of Applied Toxicology*, 3(6):272-290. 1983.**
5. **U.S. Department of Health and Human Services. Registry of Toxic Effects of Chemical Substances (RTECS, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.**
6. **U.S. Environmental Protection Agency. *Integrated Risk Information System (IRIS) on Mixed Xylenes*. Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development, Cincinnati, OH. 1993.**
7. **U.S. Environmental Protection Agency. *Integrated Risk Information System (IRIS) on m-Xylene*. Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development, Cincinnati, OH. 1993.**
8. **U.S. Environmental Protection Agency. *Integrated Risk Information System (IRIS) on o-Xylene*. Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development, Cincinnati, OH. 1993.**
9. **U.S. Environmental Protection Agency. *Integrated Risk Information System (IRIS) on p-Xylene*. Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development, Cincinnati, OH. 1993.**
10. **U.S. Environmental Protection Agency. *Health Effects Assessment Summary Tables. Annual Update*. Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development, Cincinnati, OH. 1993.**
11. **U.S. Environmental Protection Agency. *Technical Background Document to Support Rulemaking Pursuant to the Clean Air Act--Section 112(g). Ranking of Pollutants with Respect to Hazard to Human Health*. EPA-450/3-92-010. Emissions Standards Division, Office of Air Quality Planning and Standards, Research Triangle Park, NC. 1994.**

1. * This fact sheet refers to the mixture of all three isomers of mixed xylenes as "mixed mixed xylenes" and the isomers by their individual isomer names.

Xylenes

CASRN 1330-20-7

Contents

I.A. REFERENCE DOSE FOR CHRONIC ORAL EXPOSURE (RfD)

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II. CARCINOGENICITY ASSESSMENT FOR LIFETIME EXPOSURE

VI. BIBLIOGRAPHY

VII. REVISION HISTORY

VIII. SYNONYMS

0270
Xylenes; CASRN 1330-20-7

Health assessment information on a chemical substance is included in IRIS only after a comprehensive review of chronic toxicity data by U.S. EPA health scientists from several Program Offices and the Office of Research and Development. The summaries presented in Sections I and II represent a consensus reached in the review process. Background information and explanations of the methods used to derive the values given in IRIS are provided in the Background Documents.

STATUS OF DATA FOR Xylenes

File On-Line 09/30/1987

Category (section)	Status	Last Revised
Oral RfD Assessment (I.A.)	on-line	09/30/1987
Inhalation RfC Assessment (I.B.)	no data	

Carcinogenicity Assessment (II.) on-line 03/01/1991

_I. CHRONIC HEALTH HAZARD ASSESSMENTS FOR NONCARCINOGENIC EFFECTS

__I.A. REFERENCE DOSE FOR CHRONIC ORAL EXPOSURE (RfD)

Substance Name -- Xylenes
CASRN -- 1330-20-7
Last Revised -- 09/30/1987

The oral Reference Dose (RfD) is based on the assumption that thresholds exist for certain toxic effects such as cellular necrosis. It is expressed in units of mg/kg-day. In general, the RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. Please refer to the Background Document for an elaboration of these concepts. RfDs can also be derived for the noncarcinogenic health effects of substances that are also carcinogens. Therefore, it is essential to refer to other sources of information concerning the carcinogenicity of this substance. If the U.S. EPA has evaluated this substance for potential human carcinogenicity, a summary of that evaluation will be contained in Section II of this file.

___I.A.1. ORAL RfD SUMMARY

Critical Effect	Experimental Doses*	UF	MF	RfD
Hyperactivity, decreased body weight and increased mortality (males) Chronic Rat Gavage Study NTP, 1986	NOAEL: 250 mg/kg/day (converted to 179 mg/kg/day) FEL: 500 mg/kg/day (converted to 357 mg/kg/day)	100	1	2E+0 mg/kg/day

---

*Conversion Factors: Dose adjusted for gavage schedule (5\days/week).

___I.A.2. PRINCIPAL AND SUPPORTING STUDIES (ORAL RfD)

NTP (National Toxicology Program). 1986. NTP Technical Report on the Toxicology and Carcinogenesis of Xylenes (mixed) (60.2% m-xylene, 13,6% p-xylene, 17.0 ethylbenzene and 9.1% 0-xylene) (CAS No. 1330-20-7) in F344/N rats and B6C3F1 mice (gavage studies). U.S. DHHS, PHS, NIH, NTP, Research Triangle Park, NC. NTP TR 327, NIH Publ. No. 86-2583.

Groups of 50 male and 50 female Fischer 344 rats and 50 male and 50 female B6C3F1 mice were given gavage doses of 0, 250, or 500 mg/kg/day (rats) and 0, 500, or 1000 mg/kg/day (mice) for 5 days/week for 103 weeks. The animals were observed for clinical signs of toxicity, body weight gain, and mortality. All animals that died or were killed at sacrifice were given gross necropsy and comprehensive histologic examinations. There was a dose-related increased mortality in male rats, and the increase was significantly greater in the high-dose group compared with controls. Although increased mortality was observed at 250 mg/kg/day, the increase was not significant. Although many of the early deaths were caused by gavage error, NTP (1986) did not rule out the possibility that the rats were resisting gavage dosing because of the behavioral effects of xylene. Mice given the high dose exhibited hyperactivity, a manifestation of CNS toxicity. There were no compound-related histopathologic lesions in any of the treated rats or mice. Therefore, the high dose is a FEL and the low dose a NOAEL.

___I.A.3. UNCERTAINTY AND MODIFYING FACTORS (ORAL RfD)

UF -- An uncertainty factor of 100 was chosen: 10 for species-to-species extrapolation and 10 to protect sensitive individuals.

MF -- None

___I.A.4. ADDITIONAL COMMENTS (ORAL RfD)

U.S. EPA (1984) reported an RfD of 0.01 mg/kg/day, based on a rat dietary NOAEL of 200 ppm or 10 mg/kg/day as defined by Bowers et al. (1982) in a 6-month study. This NOAEL was divided by an uncertainty factor of 1000. U.S. EPA (1985, 1986) noted that this study used aged rats, loss of xylene from volatilization was not controlled, only one exposure level was used, and histopathologic examination was incomplete. An RfD of 4.31 mg/day (about 0.06 mg/kg/day) based on an inhalation study (Jenkins et al., 1970) using rats,

guinea pigs, monkeys, and dogs exposed to o-xylene at 3358 mg/cu.m, 8 hours/day, 5 days/ week for 6 weeks or at 337 mg/cu.m continuously for 90 days was derived by U.S. EPA (1985). Deaths in rats and monkeys, and tremors in dogs occurred at the highest dose, whereas no effects were observed in the 337 mg/cu.m continuous exposure group. The RfD based on the NTP (1986) study is preferable because it is based on a chronic exposure in two species by a relevant route of administration, and comprehensive histology was performed. Xylene is fetotoxic and teratogenic in mice at high oral doses (Nawrot and Staples, 1981; Marks et al., 1982), but the RfD as calculated should be protective of these effects.

___I.A.5. CONFIDENCE IN THE ORAL RfD

Study -- Medium
Data Base -- Medium
RfD -- Medium

The NTP (1986) study was given a medium confidence level because it was a well-designed study in which adequately sized groups of two species were tested over a substantial portion of their lifespan, comprehensive histology was performed, and a NOAEL was defined; but clinical chemistries, blood enzymes, and urinalysis were not performed. The data base was given a medium confidence level because, although supporting data exist for mice and teratogenicity and fetotoxicity data are available with positive results at high oral doses, a LOAEL for chronic oral exposure has not been defined. Medium confidence in the RfD follows.

___I.A.6. EPA DOCUMENTATION AND REVIEW OF THE ORAL RfD

Source Document -- U.S. EPA, 1986, 1985, 1984

The Health and Environmental Effects Profile for Xylenes (o-, m-, p-) has received limited peer review and extensive agency-wide review, 1986.

The Drinking Water Criteria Document for Xylenes has received extensive peer and agency-wide review.

The Health Effects Assessment for Xylenes has received ECAO internal review and limited agency review.

Other EPA Documentation -- None

Agency Work Group Review -- 12/05/1985, 03/19/1987

Verification Date -- 03/19/1987

___I.A.7. EPA CONTACTS (ORAL RfD)

Please contact the Risk Information Hotline for all questions concerning this assessment or IRIS, in general, at (513)569-7254 (phone), (513)569-7159 (FAX) or RIH.IRIS@EPAMAIL.EPA.GOV (internet address).

__I.B. REFERENCE CONCENTRATION FOR CHRONIC INHALATION EXPOSURE (RfC)

Substance Name -- Xylenes
CASRN -- 1330-20-7

Not available at this time.

_II. CARCINOGENICITY ASSESSMENT FOR LIFETIME EXPOSURE

Substance Name -- Xylenes
CASRN -- 1330-20-7
Last Revised -- 03/01/1991

Section II provides information on three aspects of the carcinogenic assessment for the substance in question; the weight-of-evidence judgment of the likelihood that the substance is a human carcinogen, and quantitative estimates of risk from oral exposure and from inhalation exposure. The quantitative risk estimates are presented in three ways. The slope factor is the result of application of a low-dose extrapolation procedure and is presented as the risk per (mg/kg)/day. The unit risk is the quantitative estimate in terms of either risk per ug/L drinking water or risk per ug/cu.m air breathed. The third form in which risk is presented is a drinking water or air concentration providing cancer risks of 1 in 10,000, 1 in 100,000 or 1 in 1,000,000. The rationale and methods used to develop the carcinogenicity

information in IRIS are described in The Risk Assessment Guidelines of 1986 (EPA/600/8-87/045) and in the IRIS Background Document. IRIS summaries developed since the publication of EPA's more recent Proposed Guidelines for Carcinogen Risk Assessment also utilize those Guidelines where indicated (Federal Register 61(79):17960-18011, April 23, 1996). Users are referred to Section I of this IRIS file for information on long-term toxic effects other than carcinogenicity.

__II.A. EVIDENCE FOR CLASSIFICATION AS TO HUMAN CARCINOGENICITY

___II.A.1. WEIGHT-OF-EVIDENCE CLASSIFICATION

Classification -- D; not classifiable as to human carcinogenicity.

Basis -- Orally administered technical xylene mixtures did not result in significant increases in incidences in tumor responses in rats or mice of both sexes.

___II.A.2. HUMAN CARCINOGENICITY DATA

None.

___II.A.3. ANIMAL CARCINOGENICITY DATA

Inadequate. In an NTP (1986) study, 50 male and 50 female F344/N rats were treated by gavage with mixed xylenes in corn oil (60% m-xylene, 14% p-xylene, 9% o-xylene and 17% ethylbenzene) at dosages of 0, 250 or 500 mg/kg/day, 5 days/week for 103 weeks. Similarly, 50 male and 50 female B6C3F1 mice were treated with the same xylene mixture at dosages of 0, 500 or 1000 mg/kg/day. Animals were killed and examined histologically when moribund or after 104-105 weeks. An apparent dose-related increased mortality was observed in male rats, but this difference was statistically significant for the high dose group, only. No other differences in survival between dosage groups of either sex were observed. Interstitial cell tumors of the testes could not be attributed to administration of the test compound observed in male rats (43/50 control, 38/50 low-dose and 41/49 high-dose). NTP (1986) reported that there were no significant changes in the incidence of neoplastic or nonneoplastic lesions in either the rats or mice that could be considered related to the mixed xylene treatment, and concluded that under the conditions

of these 2-year gavage studies, there was "no evidence of carcinogenicity" of xylene (mixed) for rats or mice of either sex at any dosage tested.

Maltoni et al. (1985), in a limited study, reported higher incidences (compared with controls) of malignant tumors in male and female Sprague-Dawley rats treated by gavage with xylene in olive oil at 500 mg/kg/day, 4 or 5 days/week for 104 weeks. This study did not report survival rates or specific tumor types; therefore, the results cannot be interpreted.

Berenblum (1941) reported that "undiluted" xylene applied at weekly intervals produced one tumor-bearing animal out of 40 after 25 weeks in skin-painting experiments in mice. No control groups were described. Pound (1970) reported negative results in initiation-promotion experiments with xylene as the initiator and croton oil as the promotor.

___II.A.4. SUPPORTING DATA FOR CARCINOGENICITY

The frequency of sister chromatid exchanges and chromosomal aberrations were nearly identical between a group of 17 paint industry workers exposed to xylene and their respective referents (Haglund et al., 1980). In vitro, xylene caused no increase in the number of sister chromatid exchanges in human lymphocytes (Gerner-Smidt and Friedrich, 1978). Studies indicate that xylene isomers, technical grade xylene or mixed xylene are not mutagenic in tests with Salmonella typhimurium (Florin et al., 1980; NTP, 1986; Bos et al., 1981) nor in mutant reversion assays with Escherichia coli (McCarroll et al., 1981). Technical grade xylene, but not o- and m-xylene, was weakly mutagenic in Drosophila recessive lethal tests. Chromosomal aberrations were not increased in bone marrow cells of rats exposed to xylenes by inhalation (Donner et al., 1980).

__II.B. QUANTITATIVE ESTIMATE OF CARCINOGENIC RISK FROM ORAL EXPOSURE

Not available.

__II.C. QUANTITATIVE ESTIMATE OF CARCINOGENIC RISK FROM INHALATION

EXPOSURE

Not available.

__II.D. EPA DOCUMENTATION, REVIEW, AND CONTACTS (CARCINOGENICITY ASSESSMENT)

___II.D.1. EPA DOCUMENTATION

Source Document -- U.S. EPA, 1987

The Drinking Water Criteria Document for Xylene has received Agency and external review.

___II.D.2. REVIEW (CARCINOGENICITY ASSESSMENT)

Agency Work Group Review -- 12/02/1987

Verification Date -- 12/02/1987

___II.D.3. U.S. EPA CONTACTS (CARCINOGENICITY ASSESSMENT)

Please contact the Risk Information Hotline for all questions concerning this assessment or IRIS, in general, at (513)569-7254 (phone), (513)569-7159 (FAX) or RIH.IRIS@EPAMAIL.EPA.GOV (internet address).

_VI. BIBLIOGRAPHY

Substance Name -- Xylenes
CASRN -- 1330-20-7
Last Revised -- 07/01/1989

__VI.A. ORAL RfD REFERENCES

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U.S. EPA. 1984. Health Effects Assessment for Xylene. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Emergency and Remedial Response, Washington, DC.

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U.S. EPA. 1986. Health and Environmental Effects Profile for Xylene (o-,m-,p-). Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH and the Environmental Criteria and Assessment Office, Research Triangle Park, NC for the Office of Solid Waste and Emergency Respo

__VI.B. INHALATION RfD REFERENCES

None

__VI.C. CARCINOGENICITY ASSESSMENT REFERENCES

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Bos, R.P., R.M.E. Brouns, R. Van Doorn, J.L.G. Theuws and P.Th. Henderson. 1981. Non-mutagenicity of toluene, o-, m- and p-xylene, o-methylbenzylalcohol and o-methylbenzylsulfate in the Ames assay. Mutat. Res. 88: 273-280.

Donner, M., J. Maki-Paakkanen, H. Norppa, M. Sorsa and H. Vainio. 1980. Genetic toxicology of xylenes. Mutat. Res. 74: 171-172.

Florin, I., L. Rutberg, M. Curvall and C.R. Enzell. 1980. Screening of tobacco smoke constituents for mutagenicity using the Ames' test. Toxicology. 15: 219-232.

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Maltoni, C., B. Conti, G. Cotti and F. Belpoggi. 1985. Experimental studies on benzene carcinogenicity at the Bologna Institute of Oncology: Current results and ongoing research. Am. J. Ind. Med. 7: 415-446.

McCarroll, N.E., C.E. Piper and B.H. Keech. 1981. An E. coli microsuspension assay for the detection of DNA damage induced by direct-acting and promutagens. Environ. Mutagen. 3: 429-444.

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Washington, DC. ECAO-CIN-416. Final.

_VII. REVISION HISTORY

Substance Name -- Xylenes
CASRN -- 1330-20-7

Date	Section	Description
09/26/1988	II.	Carcinogen summary on-line
07/01/1989	I.B.	Inhalation RfD now under review
07/01/1989	VI.	Bibliography on-line
03/01/1991	II.D.3.	Primary contact changed
03/01/1991	IV.F.1.	EPA contact changed
01/01/1992	I.A.7.	Secondary contact changed
01/01/1992	IV.	Regulatory actions updated
08/01/1995	I.B.	EPA's RfD/RfC and CRAVE workgroups were discontinued in May, 1995. Chemical substance reviews that were not completed by September 1995 were taken out of IRIS review. The IRIS Pilot Program replaced the workgroup functions beginning in September, 1995.
04/01/1997	III.,IV., V.	Drinking Water Health Advisories, EPA Regulatory Actions, and Supplementary Data were removed from IRIS on or before April 1997. IRIS users were directed to the appropriate EPA Program Offices for this information.

VIII. SYNONYMS

Substance Name -- Xylenes
CASRN -- 1330-20-7
Last Revised -- 09/30/1987

108-38-3
1330-20-7
2106-42-3
95-47-6
dimethylbenzene

1,2-dimethylbenzene
1,3-dimethylbenzene
1,4-dimethylbenzene
mixed xylenes
m-xylene
meta-xylene
o-xylene
ortho-xylene
p-xylene
para-xylene
Xylenes
.

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Last updated: **5 May 1998**
URL: http://www.epa.gov/iris/subst/0270.htm

Drinking Water and Health

As part of the Drinking Water and Health pages, this fact sheet is part of a larger publication:

National Primary Drinking Water Regulations

Consumer Factsheet on: XYLENES

This is a factsheet about a chemical that may be found in some public or private drinking water supplies. It may cause health problems if found in amounts greater than the health standard set by the United States Environmental Protection Agency (EPA).

What is Xylene and how is it used?

A xylene is any of a group of very similar organic compounds. They are clear liquids with a sweet odor. The greatest use of xylenes is as a solvent which is much safer than benzene. Other uses include: in gasoline as part of the BTX component (benzene-toluene-xylene); Xylene mixtures are used to make phthalate plasticizers, polyester fiber, film and fabricated items.

The list of trade names given below may help you find out whether you are using this chemical at home or work.

Trade Names and Synonyms:

Dimethyl benzene
Xylol
Methyltoluene
Violet 3

Why is Xylene being Regulated?

In 1974, Congress passed the Safe Drinking Water Act. This law requires EPA to determine safe levels of chemicals in drinking water which do or may cause health problems. These non-enforceable levels, based solely on possible health risks and exposure, are called Maximum Contaminant Level Goals.

The MCLG for xylenes has been set at 10 parts per million (ppm) because EPA believes this level of protection would not cause any of the potential health problems described below.

Based on this MCLG, EPA has set an enforceable standard called a Maximum Contaminant Level (MCL). MCLs are set as close to the MCLGs as possible, considering the ability of public water systems to detect and remove contaminants using suitable treatment technologies.

The MCL has been set at 10 ppm because EPA believes, given present technology and resources, this is the lowest level to which water systems can reasonably be required to remove

this contaminant should it occur in drinking water.

These drinking water standards and the regulations for ensuring these standards are met, are called National Primary Drinking Water Regulations. All public water supplies must abide by these regulations.

What are the Health Effects?

Short-term: EPA has found xylenes to potentially cause the following health effects when people are exposed to it at levels above the MCL for relatively short periods of time: disturbances of cognitive abilities, balance, and coordination.

Long-term: Xylenes has the potential to cause the following effects from a lifetime exposure at levels above the MCL: damage to the central nervous system, liver and kidneys.

How much Xylene is produced and released to the environment?

Production of xylenes was 6.84 billion lbs. in 1993. Major environmental releases of xylenes are due to evaporation from the refining and use of petroleum products. It may also be released by leaks or spills during the transport and storage of gasoline and other fuels. Xylenes are a natural products of many plants, and are a component of petroleum and coal tar.

From 1987 to 1993, according to EPA's Toxic Chemical Release Inventory, xylene releases to land and water totalled nearly 4.8 billion lbs. These releases were primarily from petroleum refining industries. The largest releases occurred in Texas. The largest direct releases to water occurred in New Jersey and Georgia.

What happens to Xylene when it is released to the environment?

Most of the xylenes are released into the atmosphere where they are quickly degraded by sunlight. When released to soil or water, xylenes will quickly evaporate. They may leach into ground water and persist there for several years. There is little potential for accumulation in aquatic life.

How will Xylene be Detected in and Removed from My Drinking Water?

The regulation for xylenes became effective in 1992. Between 1993 and 1995, EPA required your water supplier to collect water samples every 3 months for one year and analyze them to find out if xylenes is present above 0.5 ppb. If it is present above this level, the system must continue to monitor this contaminant.

If contaminant levels are found to be consistently above the MCL, your water supplier must take steps to reduce the amount of xylenes so that it is consistently below that level. The following treatment methods have been approved by EPA for removing xylenes: Granular activated charcoal in combination with Packed Tower Aeration.

How will I know if Xylene is in my drinking water?

If the levels of xylenes exceed the MCL, 10 ppm, the system must notify the public via newspapers, radio, TV and other means. Additional actions, such as providing alternative drinking water supplies, may be required to prevent serious risks to public health.

Drinking Water Standards:

Mclg: 10 ppm

Mcl: 10 ppm

Xylene Releases to Water and Land, 1987 to 1993 (in pounds):

		Water	Land
TOTALS (in pounds)		**875,943**	**3,897,738**
Top Ten States*			
TX	30,853	2,099,734	
NJ	294,437	280,759	
IL	36	206,990	
IN	0	145,079	
AL	34,361	59,022	
CA	0	91,500	
MI	0	86,774	
GA	68,310	15,000	
VA	50,100	33,000	
WA	27,860	52,360	
Major Industries*			
Petroleum refining		131,817	2,678,958
Metal barrels, drums		5	289,542
Textile finishing, misc.		278,454	0
Misc. Industrial chems.		95,706	69,696
Extruded Aluminum prod.		1,265	138,798
Furniture, fixtures		0	91,500
Cotton fabric finishing		68,310	15,000
Wood office furniture		0	67,677
Pharmaceuticals		52,285	3,100
Paper mills		52,480	2,122

* Water/Land totals only include facilities with releases greater than a certain amount - usually 1000 to 10,000 lbs.

Learn more about your drinking water!

EPA strongly encourages people to learn more about their drinking water, and to support local efforts to protect and upgrade the supply of safe drinking water. Your water bill or telephone books government listings are a good starting point.

Your local water supplier can give you a list of the chemicals they test for in your water, as well as how your water is treated.

Your state Department of Health/Environment is also a valuable source of information.

For help in locating these agencies or for information on drinking water in general, call: EPAs Safe Drinking Water Hotline: (800) 426-4791.

For additional information on the uses and releases of chemicals in your state, contact the: Community Right-to-Know Hotline: (800) 535-0202.

Search EPA OGWDW Home Office of Water Comments

Revised *January 26, 1998*

Office of Ground Water and Drinking Water

http://www.epa.gov/OGWDW/dwh/c-voc/xylenes.html

Level 1

Chemical Name: Xylenes

CAS Registry Number: 1330-20-7

Click on red circle(s) to obtain data.

Risk Value	ATSDR	Health Canada	ITER	RIVM	U.S.EPA	WHO/IPCS
Noncancer Oral	●	●	●	●	●	●
Cancer Oral	●	●	●	●	●	●
Noncancer Inhalation	●	●	●	●	●	●
Cancer Inhalation	●	●	●	●	●	●

Glossary of ITER definitions

ITER Instructions

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Toxicology Excellence for Risk Assessment

TERA

NTP CHEMICAL REPOSITORY (RADIAN CORPORATION, AUGUST 29, 1991)
XYLENES (MIXED)

-IDENTIFIERS
 ===========

*CATALOG ID NUMBER: 001205

*CAS NUMBER: 1330-20-7

*BASE CHEMICAL NAME: XYLENES,MIXED

*PRIMARY NAME: XYLENES (MIXED)

*CHEMICAL FORMULA: C8H10

*STRUCTURAL FORMULA: C6H4(CH3)2

*WLN: 1R X

*SYNONYMS:
  COMPONENT 1 (83%): XYLENES
                     DIMETHYLBENZENES
                     XYLOL
  COMPONENT 2 (17%): ETHYL BENZENE

-PHYSICAL CHEMICAL DATA
 ======================

*PHYSICAL DESCRIPTIONS: LITERATURE: Colorless liquid
                        REPOSITORY: Colorless liquid

*MOLECULAR WEIGHT: 106.17

*SPECIFIC GRAVITY: 0.860 @ 20/4 C [269,274]

*DENSITY: Not available

*MP (DEG C): Not available

*BP (DEG C): 137-144 C [053,269,274]

*SOLUBILITIES:
       WATER : <1 mg/mL @ 22 C (RAD)

        DMSO : >=100 mg/mL @ 22 C (RAD)

 95% ETHANOL : >=100 mg/mL @ 22 C (RAD)

    METHANOL : Not available

     ACETONE : >=100 mg/mL @ 22 C (RAD)

     TOLUENE : Not available

*OTHER SOLVENTS:
  Absolute alcohol: Miscible [031]
  Ether: Soluble [062]
  Organic solvents: Miscible [421]

*VOLATILITY:
Vapor pressure: 6.72 mm Hg @ 21 C [042]; 10 mm Hg @ 28 C [053]
Vapor density : 3.7

*FLAMMABILITY(FLASH POINT):
This chemical has a flash point of 25.6 C (78 F) (RAD). It is flammable. Fires involving this material can be controlled with a dry chemical, carbon dioxide or Halon extinguisher. The autoignition temperature for this compound is 466 C (870 F) [058].

*UEL: 7.0% [036,053] LEL: 1.0 % [036,053]

*REACTIVITY:
This compound reacts with oxidizing agents [042,053,269]. It will attack some forms of plastics, rubber and coatings. It readily dissolves fats, oils and waxes [430].

*STABILITY:
This compound is stable under normal laboratory conditions. Solutions of this chemical in water, DMSO, 95% ethanol or acetone should be stable for 24 hours under normal lab conditions (RAD).

*OTHER PHYSICAL DATA:
Refractive index: 1.4970 @ 20 C
Aromatic odor

-TOXICITY
========

*NIOSH REGISTRY NUMBER: ZE2100000

*TOXICITY:

typ. dose	mode	specie	amount	unit	other
TCLo	ihl	hmn	200	ppm	
LCLo	ihl	man	10000	ppm/6H	
LD50	orl	rat	4300	mg/kg	
LC50	ihl	rat	5000	ppm/4H	
LD50	scu	rat	1700	mg/kg	
LD50	ipr	mus	1548	mg/kg	
LDLo	ipr	gpg	2000	mg/kg	
LDLo	ipr	mam	2000	mg/kg	
LCLo	ihl	gpg	450	ppm	
LDLo	orl	hmn	50	mg/kg	

*AQTX/TLM96: 100-10 ppm

*SAX TOXICITY EVALUATION:
THR = MODERATE via inhalation and oral routes.

*CARCINOGENICITY:
Review: IARC Cancer Review: Human Inadequate Evidence
IARC Cancer Review: Animal Inadequate Evidence
IARC: Not classifiable as a human carcinogen (Group 3) [610]
Status: NTP Carcinogenesis Studies (Gavage); No Evidence: Male and Female Rat, Male and Female Mouse [620]

*MUTATION DATA:

test	lowest dose	test	lowest dose

```
    cyt-smc        1 mmol/tube        |

*TERATOGENICITY:
  Reproductive Effects Data:
   TCLo: ihl-rat   1000 mg/m3/24H (9-14D preg)
   TCLo: ihl-rat     50 mg/m3/6H (1-21D preg)
   TCLo: ihl-rat    600 mg/m3/24H (7-15D preg)
   TDLo: orl-mus  20600 ug/kg (6-15D preg)
   TCLo: ihl-mus   4000 ppm/6H (6-12D preg)
   TDLo: orl-mus     31 mg/kg (6-15D preg)
   TCLo: ihl-mus   2000 ppm/6H (6-12D preg)

*STANDARDS, REGULATIONS & RECOMMENDATIONS:
  OSHA: Federal Register (1/19/89) and 29 CFR 1910.1000 Subpart Z
        Transitional Limit: PEL-TWA 100 ppm [610]
        Final Limit: PEL-TWA 100 ppm; STEL 150 ppm [610]
  ACGIH: TLV-TWA 100 ppm; STEL 150 ppm [610]
  NIOSH Criteria Document: Recommended Exposure Limit to this compound-air:
                           TWA 100 ppm; Ceiling Limit 200 ppm/10M [015,610]
  NFPA Hazard Rating: Health (H): 2
                      Flammability (F): 3
                      Reactivity (R): 0
  H2: Materials hazardous to health, but areas may be entered freely with
      full-faced mask self-contained breathing apparatus which provides
      eye protection (see NFPA for details).
  F3: Materials which can be ignited under almost all normal temperature
      conditions (see NFPA for details).
  R0: Materials which are normally stable even under fire exposure conditions
      and which are not reactive with water (see NFPA for details).

*OTHER TOXICITY DATA:
  Skin and Eye Irritation Data:
    eye-hmn  200  ppm
    skn-rbt  100% MOD
    skn-rbt  500  mg/24H MOD
    eye-rbt   87  mg MLD
    eye-rbt    5  mg/24H SEV
  Standards and Regulations: DOT-Hazard: Flammable liquid; Label: Flammable
                              liquid
                             DOT-IMO: Flammable or Combustible liquid; Label:
                              Flammable liquid
  Status: NIOSH Analytical Methods: see hydrocarbons, aromatic, 1501
          EPA TSCA Chemical Inventory, 1986
          EPA TSCA 8(a) Preliminary Assessment Information, Final Rule
          EPA Genetox Program 1986, Negative: In vitro SCE-human lymphocytes;
           In vitro SCE-human
          EPA TSCA Test Submission (TSCATS) Data Base, December 1986
          Meets criteria for proposed OSHA Medical Records Rule


-OTHER DATA (Regulatory)
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*PROPER SHIPPING NAME (IATA): Xylenes

*UN/ID NUMBER: UN1307

*HAZARD CLASS: 3             SUBSIDIARY RISK: None    PACKING GROUP: III

*LABELS REQUIRED: Flammable liquid
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*PACKAGING: PASSENGER: PKG. INSTR.: 309, Y309 MAXIMUM QUANTITY: 60 L, 10 L
CARGO : PKG. INSTR.: 310 MAXIMUM QUANTITY: 220 L

*SPECIAL PROVISIONS: None

*USES:
Aviation gasoline; protective coatings; solvent for alkyd resins, lacquers, enamels, rubber cements; synthesis of organic chemicals; manufacturing dyes, sterilizing catgut; with Canada balsam as oil-immersion in microscopy and cleaning agent in microscopic technique.

*COMMENTS: Not available

-HANDLING PROCEDURES

*ACUTE/CHRONIC HAZARDS:
When heated to decomposition, this compound emits toxic fumes of CO and CO2 [269]. It can be narcotic in high concentrations [031,051,053,269]. It causes eye, nose and throat irritation [346].

*MINIMUM PROTECTIVE CLOTHING: Not available

*RECOMMENDED GLOVE MATERIALS:
Recommended Glove Type For Use With Neat (Undiluted) Chemical:
Recommendations based on permeation test results are made for handling the neat (undiluted) chemical. If this chemical makes direct contact with your glove, or if a tear, puncture or hole develops, replace them at once.

Suggested Glove Type (RAD)	Model Number	Thickness	Breakthrough Time
PVA	Edmont 29-250	0.84 mm	480 min.
Viton	North F-091	0.41 mm	480 min.

*RECOMMENDED RESPIRATOR:
Where the neat test chemical is weighed and diluted, wear a NIOSH-approved half face respirator equipped with an organic vapor/acid gas cartridge (specific for organic vapors, HCl, acid gas and SO2) with a dust/mist filter.

*OTHER: Not available

*STORAGE PRECAUTIONS:
You should store this chemical in an explosion-proof refrigerator and keep it away from oxidizing materials. STORE AWAY FROM SOURCES OF IGNITION.

*SPILLS AND LEAKAGE:
If you spill this chemical, FIRST REMOVE ALL SOURCES OF IGNITION. Then, use absorbent paper to pick up all liquid spill material. Your contaminated clothing and absorbent paper should be sealed in a vapor-tight plastic bag for eventual disposal. Solvent wash all contaminated surfaces with 60-70% ethanol followed by washing with a soap and water solution. Do not reenter the contaminated area until the Safety Officer (or other responsible person) has verified that the area has been properly cleaned.

*DISPOSAL AND WASTE TREATMENT: Not available

-EMERGENCY PROCEDURES

*SKIN CONTACT:
IMMEDIATELY flood affected skin with water while removing and isolating all contaminated clothing. Gently wash all affected skin areas thoroughly with soap and water.
If symptoms such as redness or irritation develop, IMMEDIATELY call a physician and be prepared to transport the victim to a hospital for treatment.

*INHALATION:
IMMEDIATELY leave the contaminated area; take deep breaths of fresh air. If symptoms (such as wheezing, coughing, shortness of breath, or burning in the mouth, throat, or chest) develop, call a physician and be prepared to transport the victim to a hospital.
Provide proper respiratory protection to rescuers entering an unknown atmosphere. Whenever possible, Self-Contained Breathing Apparatus (SCBA) should be used; if not available, use a level of protection greater than or equal to that advised under Respirator Recommendation.

*EYE CONTACT:
First check the victim for contact lenses and remove if present. Flush victim's eyes with water or normal saline solution for 20 to 30 minutes while simultaneously calling a hospital or poison control center.
Do not put any ointments, oils, or medication in the victim's eyes without specific instructions from a physician.
IMMEDIATELY transport the victim after flushing eyes to a hospital even if no symptoms (such as redness or irritation) develop.

*INGESTION:
DO NOT INDUCE VOMITING. If the victim is conscious and not convulsing, give 1 or 2 glasses of water to dilute the chemical and IMMEDIATELY call a hospital or poison control center. Be prepared to transport the victim to a hospital if advised by a physician.
If the victim is convulsing or unconscious, do not give anything by mouth, ensure that the victim's airway is open and lay the victim on his/her side with the head lower than the body. DO NOT INDUCE VOMITING. IMMEDIATELY transport the victim to a hospital.

*SYMPTOMS:
Symptoms of exposure to this material include irritation of the eyes, nose and throat; drying and defatting of the skin which may lead to dermatitis; chemical pneumonitis, pulmonary edema, hemorrhage, central nervous system depression, dizziness, staggering, drowsiness, unconsciousness, anorexia, nausea, vomiting and abdominal pain [346]. It may be narcotic in high concentrations [031,051,053,269]. It may also cause headache, fatigue, lassitude, irritability and gastrointestinal disturbances [421]. It can also cause reversible eye damage, a burning sensation in the mucous membranes, salivation, bloody vomit, impaired motor coordination, slurred speech, ataxia, stupor, coma, tremors, shallow respiration, ventricular irregularities, paralysis and convulsions [301]. It causes eye irritation and foggy vision [099].

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Web Sites

that offer searchable chemical databases, recommended by Scorecard

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If you want more detailed information about a chemical than Scorecard provides, there are several on-line and library resources Scorecard recommends for further research.

ON-LINE CHEMICAL DATABASES

CambridgeSoft Chemfinder
http://chemfinder.camsoft.com/

Search

Chemfinder gives basic physico-chemical data and molecular structures for chemicals, and provides links to international data sources addressing specific chemicals.

Hazardous Substances Data Bank
http://toxnet.nlm.nih.gov/

Search

HSDB focuses on the toxicology of potentially hazardous chemicals, and includes peer-reviewed information on human exposure, industrial hygiene, emergency handling procedures, environmental fate, and regulatory requirements.

University of Akron Hazardous Chemicals Database
http://ull.chemistry.uakron.edu/erd/

Search

The Hazardous Chemicals Database provides physical data on chemicals and links to Department of Transportation safety guides that are valuable for emergency response.

BIBLIOGRAPHIC RESOURCES ON CHEMICAL TOXICITY

Scorecard provides qualitative summaries of the health hazards posed by a chemical (e.g., it is a suspected neurotoxicant), but not direct access to supporting toxicological data. These scientific studies are abstracted in several toxicity databases, which are available in libraries, from commercial vendors, and sometimes on-line. The major toxicity databases include:

The Registry of Toxic Effects of Chemicals Substances (RTECS)
RTECS is a database of toxicological information compiled by the National Institute for Occupational Safety and Health. It contains summary information about the types of health effects chemicals can cause and the concentrations at which toxicity is known to occur. It is available from several commercial vendors at http://www.cdc.gov/niosh/rtecs.html, and can often be found at major public or university libraries.

TOXLINE
Free access to the National Library of Medicine's toxicology-specific database of abstracts, reference journal articles, and reports is available at http://www.medscape.com/misc/FormToxlineInfLive.html

MEDLINE

Free access to the National Library of Medicine's MEDLINE database of more than 9 million references to articles published in 3800 biomedical journals is available at http://www.nlm.nih.gov/databases/freemedl.html. Two Web-based products, PubMed and Internet Grateful Med, provide this access. Medline can also be accessed at http://www.medscape.com/misc/FormMedlineInfLive.html

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ISOPROPYL ALCOHOL (67-63-0)

summary from the About the Chemicals section of Scorecard

- **Human Health Hazards**

  Recognized: --

  Suspected:

	Reference(s)
Cardiovascular or Blood Toxicant	RTECS
Developmental Toxicant	OEHHA-2000
Gastrointestinal or Liver Toxicant	RTECS
Kidney Toxicant	OEHHA-2000
Neurotoxicant	RTECS
Respiratory Toxicant	OEHHA-AREL RTECS
Skin or Sense Organ Toxicant	OEHHA-AREL

- **Hazard Rankings**

  More hazardous than most chemicals in 1 out of 8 ranking systems.

- **Chemical Use Profile**

  This is a high volume chemical with production exceeding 1 million pounds annually in the U.S.
  Used in at least 14 industries.
  Used in consumer products, building materials or furnishings that contribute to indoor air pollution.
  Used in pesticide products.

- **Profile of Environmental Release and Waste Generation**

  No data on environmental releases in Scorecard.

- **Regulatory Coverage**

  On at least 3 federal regulatory lists.

- **Basic Testing to Identify Chemical Hazards**

  Eight basic tests to identify chemical hazards have been conducted and are publicly available for this chemical.

- **Information Needed for Safety Assessment**

  Lacks at least some of the national data required for safety assessment.
  Scorecard has risk assessment data for this chemical.

- **Links**

  Other web sites specific to this chemical:

  - CalEPA Air Resources Board Toxic Air Contaminant Summary

- IPCS International Chemical Safety Card
- National Toxicology Program Health and Safety Information Sheet
- New Jersey Fact Sheet

If none of these sources meet your needs, you can try searching some other chemical database Web sites.

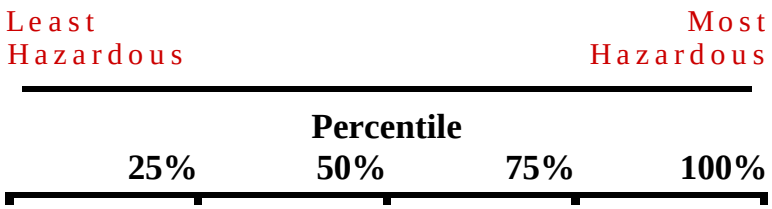
- **Notes**

  This is not a TRI chemical even though TRI uses this CAS. See the chemical profile for ISOPROPYL ALCOHOL (STRONG ACID PROCESS) for information on the form of isopropyl alcohol on the TRI list.

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Hazard Rankings

for ISOPROPYL ALCOHOL (67-63-0) from Scorecard



Human Health Rankings

Toxicity only

- Human Health Effects Score (UTN)

Toxicity and exposure potential

- Noncancer Risk Score - Air Releases (EDF)
- Noncancer Risk Score - Water Releases (EDF)
- Worker Exposure Hazard Score (IRCH)

Ecological Health Rankings

Toxicity only

- Ecological Effects Score (UTN)

Toxicity and persistence

- Environmental Hazard Value Score (IRCH)

Integrated Environmental Rankings

Combined human and ecological scores

- Total Hazard Value Score (IRCH)
- Total Hazard Value Score (UTN)

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Industrial Uses

for ISOPROPYL ALCOHOL (67-63-0) from Scorecard

This is a high volume chemical with production exceeding 1 million pounds annually in the U.S.

Which Industries Use This Chemical?	How is the Chemical Used in This Industry?
Circuit Board Manufacture	Imaging Photodevelopers
Electroplating	Electroplating - Cold-cleaning Solvents
Heat Transferring Agents	Secondary Coolants
Laboratory Chemicals	Solvents - Dilution
Laboratory Chemicals	Solvents - Extraction
Machinery Mfg and Repair	Solvents - Machinery Manufacture and Repair
Metal Degreasing	Solvents - Metal Degreasing
Paint Manufacture	Alcohol Solvents - Paint
Paint Stripping	Solvents - Paint Stripping
Pharmaceuticals Mfg	Solvents - Pharmaceuticals
Printed Circuit Board Manufacturing	Hot Air Solder Leveling-Print Circ Brd Mfg
Printed Circuit Board Manufacturing	Making PCB Holes Conductive
Printed Circuit Board Manufacturing	Outer Layer Etch/Plate - Print Circ Brd Mfg
Printing	Cleaning Solvents - Printing
Printing	Solvents for Equipment Cleaning
Printing	Solvents for Flexography
Printing	Solvents for Gravure Printing
Printing	Solvents for Lithography
Reprographic Agents	Diazotype Materials - Misc. Chemicals
Rubber Manufacture	Solvents - Rubber Manufacture
Semiconductors	Cleaning - Semiconductors
Semiconductors	Developers - Negative
Semiconductors	Developers - Positive
Unspecified	Antifreezing Agents

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Consumer Products

that contain ISOPROPYL ALCOHOL (67-63-0) from Scorecard

What kinds of consumer products may contain this chemical?

- Acid nonhousehold metal cleaners (liquid)
- Aerosol paint concentrates
- Aftershave preparations (all forms)
- Agricultural chemicals
- Antiacne preparations
- Antifreeze preparations
- Antifungal preparations
- Architectural coatings
- Auto, other transportation, and machinery refinish paints incl primers
- Automobile body polish and cleaners
- Automotive windshield washer fluid
- Bathroom tub and tile cleaners
- Body lotions
- Chemical products for pools, hot tubs, etc.
- Cleansing creams
- Cleansing lotions
- Deodorants/air fresheners (non-personal, aerosol)
- Deodorants/air fresheners (non-personal, non-aerosol)
- Disinfectants (nonagricultural)
- Emollients and protectives, including burn remedies and ointment bases
- Epoxy adhesives
- External analgesics and counterirritants
- External analgesics and counterirritants (liquid)
- External analgesics and counterirritants (ointments, pastes, creams, etc.
- Eye and ear pharmaceutical preparations
- Fabric softeners (liquid)
- Facial scrubs and masks
- Flexographic inks
- Floor polish
- Floor polish: liquid non-emulsion
- Fungicides for agric., garden and health service use
- Furniture polish and cleaners

- General antibacterials and antieptics
- General performance sealants (PVAC, butyl, vinyl, etc.)
- Glass window cleaning preparations
- Ground/traffic marking coatings
- Hair coloring preparations (bleaches, dyes, rinses, tints, etc.)
- Hair dressings incl brilliantines, creams, pomades
- Hair preparations (including shampoos)
- Hair tonics incl hair and scalp conditioners (consumer use)
- Hairspray (aerosol)
- Hairspray (non-aerosol)
- Herbicides for agric., garden and health service use
- Household alkaline machine dishwashing detergents (liquid)
- Household dry automatic dishwashing detergents
- Household hard surface cleaners (aerosol)
- Household hard surface cleaners (dry)
- Household hard surface cleaners (liquid)
- Household laundry presoaks
- Household liquid laundry detergents
- Household pesticides
- Household rug and upholstery cleaners
- Industrial particleboard (furniture, fixtures, cabinets, etc.)
- Insect repellants for human use
- Insecticides for agric., garden and health service use
- Insecticides for crawling insects
- Insecticides for flying insects
- Laundry starch preparations
- Leather dressings and finishes (excl shoe polish)
- Lubricating oils
- Miscellaneous agricultural/pesticidal products
- Miscellaneous paint-related products
- Moisturizing creams
- Nail enamel and polish removers
- Nail enamels and polishes
- Nonhousehold machine dishwashing detergents (liquid)
- Nonhousehold synthetic detergents (liquid, cationic or amphoteric base)
- Nonstructural caulking compounds and sealants
- Other alkaline household detergents

- Other alkaline nonhousehold detergents (liquid)
- Other alkaline nonhousehold dry detergents
- Other art materials incl clay, water & tempera colors, finger paint, etc.
- Other automotive chemicals
- Other cosmetics and toiletries
- Other dermatological preparations
- Other flexographic inks
- Other gravure inks
- Other hair preparations, including heat setting wave solutions
- Other indust. product finishes excl. pigment dispersions & ink vehicles
- Other industrial chemical specialty products
- Other laundry aids, icluding ironing aids and dry cleaning spotting pre
- Other lotions and oils, excl hair, shaving, and bath
- Other manicuring preparations
- Other miscellaneous allied paint products, including brush cleaners
- Other pharmaceutical preparations acting on the skin
- Other polishing preparations and related products
- Other soaps incl mechanics and medicated (bars, liquid and paste)
- Other specialty cleaning and sanitation products
- Oven cleaners
- Packaging inks: solvent types
- Packaging inks: water types
- Paint and varnish removers
- Paint thinners
- Paints and allied products
- Perfumes, toilet water, and colognes
- Pet flea and tick products, including collars
- Pharmaceutical preparations
- Pharmaceuticals for veterinary use
- Premoistened towelettes, incl wipes for babies
- Repellants and attractants
- Rubbing alcohol
- Rug and upholstery cleaners
- Shampoos
- Shoe polishes and cleaners
- Specialty performance sealants
- Suntan lotions and oils

- Synthetic resin and rubber adhesives
- Textile finishes
- Toilet bowl cleaners
- Toilet preparations
- Toilet soap excl medicated soaps (liquid)
- Topical antibiotic preparations
- Wood office furniture

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Pesticidal Uses

for ISOPROPYL ALCOHOL (67-63-0) from Scorecard

This is a high volume chemical with production exceeding 1 million pounds annually in the U.S.

List of Brand Name Products which Contain this Chemical	Percentage by Mass
ISOPROPYL ALCOHOL N.F. 99%	99%
ISOPROPYL ALCOHOL 99%	99%
ISOPROPYL ALCOHOL N. F. 99%	99%
DENSCO TEK-TEX (CHAIRSIDE)	91.37%
ISOPROPYL ALCOHOL 91%	91%
ISOPROPYL ALCOHOL 91%	91%
BACTACIDE-M	90%
BACTACIDE-M	90%
ACE LIQUID ALGAECIDE	89.8%
HILL'S HOLIDAY FLEA & TICK PUMP SPRAY	89.5%
CALGON NO. 22 ALGAECIDE	89%
PET'S BEST MANGE LOTION	80.43%
SANITIZED TPO FOR INDUSTRIAL USE ONLY	78%
SANITIZED LBS	78%
SANITIZED CPO FOR INDUSTRIAL USE ONLY	78%
DISINFECTANT PUMP SPRAY	75.71%
MEDI-Q DISINFECTANT DEODORANT AIR REFRESHENER	75.71%
HY-TEST MILDEW SPRAY	71.4%
VIRAHOL	70%
VIRAHOL TOWELETTE	70%
THERMO BENZ THERMOMETER WIPE	70%
TOMAC SENTRY THERMOMETER KIT	70%
HOSPITAL DISINFECTANT	69.52%
LEMON SCENTED HOSPITAL DISINFECTANT	67.5%
KLEAN AIR T.M. BRAND HUMIDIFIER BACTERIOSTAT	66%
CARCOSTAT TBO 8%	65%
BLITZ AIR SANITIZER AND DEODORANT	65%
PURSUE DISINFECTANT SPRAY	64.95%
ESCO 512	63.5%

ISOTEX 70 DISINFECTING TOWELETTES	63.25%
ISOTEX 70 DISINFECTING TOWELETTES	63.25%
DISCIDE ULTRA DISINFECTING SPRAY	63.25%
FARMADE BENDANE	61%
NO. 46 SPRAY-ZENE	60.72%
STERI-FAB BACTERICIDE-SANITIZER-FUNGICIDE-INSECTICIDE-DEODORANT-GERMIC	60.39%
STERI-FAB	60.39%
SOLU STYRIL GERMICIDE SOLUTION	60%
BOWSTERAL ANTI RUST DISINFECTANT	60%
ESCO 500	60%
VIRO-PHENE	60%
GERMEX DISINFECTANT-DEODORANT BACTERICIDAL-FUNGICIDAL	60%
PRESTIGE SPRAY DISINFECTANT	59.16%
MIST OF KINGS NON-SELECTIVE DISINFECTANT HOSPITAL GRADE	59.16%
NATIONAL CHEMSEARCH PROMINE-A DISINFECTANT DEODORANT	57%
BARCOLENE SPRAY DISINFECTANT	56.41%
COREXIT 7675 BACTERICIDE	56%
SANI-CLOTH GERMICIDAL WIPES	55%
CHAMPION SPRAYON DISINFECTANT FORMULA 4	55%
DOUBLE ACTION SPRAYFECT DISINFECTANT DEODORIZER	54.79%
VIRO CERF POWERFUL HOSPITAL DISINFECTANT LONG LASTING DEODORIZER	53.46%
SOLAR-QUAT SPRAY A-36-S	53%
MAGIC GUARD DISINFECTANT SPRAY	53%
LICO DDS SPRAY DISINFECTANT-DEODORIZER-AIRFRESHNER	53%
ACCRA PAC AEROSOL SURFACE DISINFECTANT	53%
BIOTECH SURFACE DISINFECTANT SPRAY	53%
FRESH N KLEEN	53%
HI COSAN SPRAY DISINFECTANT	53%
DDQ SURFACE DISINFECTANT	53%
AEROSOL SURFACE DISINFECTANT	53%
DISINFECTANT DEODORANT & AIR REFRESHENER	53%
SCAN-X	53%
BIOTECH SURFACE DISINFECTANT SPRAY	53%

DISINFECTANT DEODORANT	53%
BIG D DISINFECTANT & DEODORANT	53%
BUTCHER'S CLOCKWORK DISINFECTANT DEODORIZER SPRAY	53%
RITE OFF SURFACE DISINFECTANT AND DEODORANT	53%
AEROSOL DISINFECTANT	53%
NEW AKTAIRE SURFACE DISINFECTANT & AIR SANIT.DEOD. SPRAY	53%
CONTACT HOSPI SPRAY DISINFECTANT	53%
AEROSAN SPRAY DISINFECTANT	53%
SPRAYON AIR REFRESHENER DEODORIZER DISINFECTANT SPRAY	53%
CRAIN'S G-GO HOSPITAL DISINFECTANT DEODORANT	53%
ENVICIDE II	53%
QUATRICIDE SURFACE DISINFECTANT AND AIR SANITIZER DEODORIZOR SPRAY	53%
HOLCOMB SPACE AND SURFACE DISINFECTANT/DEODORANT	53%
SPRAY PAK DISINFECTANT DEODORIZER AIR REFRESHENER	53%
HOSPITAL DISINFECTANT DEODORANT	52.92%
MICRO X MINT DISINFECTANT	52.92%
MICRO -X BOUQUET DISINFECTANT	52.92%
MICRO-X ORANGE DISINFECTANT	52.92%
MICRO-X LEMON DISINFECTANT	52.92%
MICRO X MINT DISINFECTANT	52.92%
MICRO -X BOUQUET DISINFECTANT	52.92%
MICRO-X ORANGE DISINFECTANT	52.92%
MICRO-X LEMON DISINFECTANT	52.92%
BIO-GUARD ORANGE FRAGRANT SURFACE SPRAY DISINFECTANT	52.92%
BIO-GUARD SPICY FRAGRANT SURFACE SPRAY DISINFECTANT	52.92%
BIO-GUARD LEMON SCENTED SURFACE SPRAY DISINFECTANT	52.92%
BIO-GUARD MINT FRAGRANT SURFACE SPRAY DISIN.FUNG.DEOD.	52.92%
MICRO X MINT DISINFECTANT	52.92%
MICRO -X BOUQUET DISINFECTANT	52.92%
MICRO-X ORANGE DISINFECTANT	52.92%
DEL BAC OFF GERMICIDAL, SANITIZER, DEODORIZER	52.7%
FINAST DISINFECTANT SPRAY	52.37%
MISTY SURFACE DISINFECTANT AND AIR DEODORIZER	52.22%
BIOTECH DISINFECTANT SURFACE SPRAY P220	51.08%

BIOTECH DISINFECTANT SURFACE SPRAY P220	51.08%
STEWARD SPRAY DISINFECTANT	51%
BIOTECH DISINFECTANT SURFACE SPRAY Q500	50.3%
BIOTECH DISINFECTANT SURFACE SPRAY Q500	50.3%
STAF HOSPITAL SPRAY DISINFECTANT	50.2%
AM-43	50%
BIOHIBIT B-708	50%
STERI-SOL GERMICIDAL SOLUTION	50%
MICROBIOCIDE RPC-3491	50%
INCUBATOR FUMIGANT	49%
NEW MICROJET CONCENTRATE	47%
P B F SHOE SPRAY	46.44%
NICE AIR SANITIZER	45.75%
CLIPPERCIDE SPRAY	45.63%
ACCRA PAC	45.42%
GLYTONE AIR SANITIZER	45%
GLYCO-CIDE AIR SANITIZER-DEODORANT	45%
HERPECIDAL SPRAY	44%
GERMICIDAL SOLUTION	44%
MICRO-KILL LEMON FRAGRANCE SPRAY DISINFECTANT	43.22%
MICRO-KILL ORANGE FRAGRANCE SPRAY DISINFECTANT	43.22%
MICRO-KILL MINT FRAGRANCE SPRAY DISINFECTANT	43.22%
SPEER HOSPITAL SPRAY DISINFECTANT/DEODORANT	43.22%
BIO-GUARD BQ-25 HOSPITAL SPRAY	43.22%
BIO-GUARD OT-25 HOSPITAL SPRAY	43.22%
BIO-GUARD SL-25 SPRAY DISINFECTANT	43.22%
SAFARI BOUQUET FRAGRANCE AIR SANTIZER DEODORIZER	43.22%
MINTEX MINT FRAGRANCE AIR SANITIZER DEODORIZER	43.22%
LEMONEX LEMON FRAGRANCE AIR SANITIZER DEODORIZER	43.22%
SAFARI BOUQUET FRAGRANCE AIR SANTIZER DEODORIZER	43.22%
SAFARI ORANGE FRAGRANCE AIR SANITIZER DEODORIZER	43.22%
MINTEX MINT FRAGRANCE AIR SANITIZER DEODORIZER	43.22%
LEMONEX LEMON FRAGRANCE AIR SANITIZER DEODORIZER	43.22%
SAFARI ORANGE FRAGRANCE AIR SANITIZER DEODORIZER	43.22%
BIO-GUARD MT-25 HOSPITAL SPRAY	43.22%

BIO GUARD SL-25 HOSPITAL SPRAY DISINFECTANT AND DEODORANT	43.22%
MICRO-KILL BOUQUET FRAGRANCE SPRAY DISINFECTANT	43.22%
NATIONAL CHEMSEARCH QUA-TA-SEPT	42%
ALGAECIDE-BIOCIDE	40.4%
M-80T ALGAECIDE	40.4%
M-80T ALGAECIDE	40.4%
HERPICIDE SPRAY	40%
GERMICIDE TINCTURE 1 750	40%
JUNGLE-JEL	40%
BENZALKONIUM CHLORIDE U.S.P. TINCTURE SOLUTION	40%
BENZALKONIUM CHLORIDE TINCTURE SOLUTION 1:750	40%
GESCO FLY-FREE GEL	40%
BIOMET 600 DISINFECTANT AND DEODORIZER FOR SURFACES	39.02%
STAPH-600 DISINFECTANT DEODORANT FOR SURFACES	39.02%
NATIONAL CHEMSEARCH TRI-GLY AIR SANITIZER & DEODORANT	38.5%
PURE MINT ODOR DISINFECTANT	38%
R. I. P. ANT AND ROACH INSECTICIDE WITH REPELLENT	37.5%
FUZZIE BUDDIE SPRAY FOR PETS WITH PURE EUCALYPTUS OIL	37.5%
SURFLO -B33	37.4%
BENZALKONIUM CHLORIDE TINCTURE SOLUTION 1:750	37%
SANI-SPEED GERMICIDAL SOLUTION	35.52%
SANICO AIR-MIST ODORLESS	35.45%
SANICO'S AIR-MIST STRAWBONAL	35.18%
NYCO WINTERGREEN DISINFECTANT & DEODORANT	35%
PROP-O-SURG	34.96%
BIOMET 2 ANTIMICROBIAL COMPOUND	34.9%
GLYCO AIRE	34.75%
NEW SPRAY DISINFECTANT BY MEADOW	34.39%
ANI-SHIELD	33.1%
SELIG'S BANO 5AW	33%
SELIG'S BANO GAW	33%
GLYCOLIN AIR SPRAY DISINFECTANT DEODORANT	32%
SPRAYPAK SPRAY DISINFECTANT	30.8%
LEPPCO BRAND FLORASCENT	30.8%
GRIFFIN'S FRESH-ETTE	30.8%

BETZ ENTEC 342	30%
NALCON 7610	30%
NALCO NO. 25 L	30%
NALCO 321	30%
NALCO 431 MICROORGANISM CONTROL CHEMICAL	30%
GLYCOLENE	30%
BETZ BC-102 SLIMICIDE	30%
WRICO DMC	30%
BABBIT INSTITTL GLYCOL AIR SANITIZER & RM DEODORANT MINT SCENTED	30%
BABBIT INSTITUTIONAL GLYCOL AIR SANITIZER & ROOM DEODORANT	30%
ANTI GERM-55 DISINFECTANT SANITIZER DEORANT	30%
NALCO 425-L MICROORGANISM CONTROL CHEMICAL	30%
BABBIT INSTITTL GLYCOL AIR SANTZZR & RM DEODRNT APPLE BLSSM SCENT	30%
SALON CONCENTRATED SANITIZER DEODORIZER DISINFECTANT	30%
M-K-C GLYCOL VAPAIR	30%
SURGISEPT VIRUCIDE GERMICIDE CONCENTRATE	29.3%
INVADE DOES IT DESTROYS MOST BACTERIA AND ODORS	29.2%
FLAIR	29.2%
CERTIFIED NEW GLY-SAN	29.2%
PINOX 39	28.57%
MICRO PINE PINE ODOR DISINFECTANT COEF.39	28.57%
PINOX 39	28.57%
PINOX 39	28.57%
BIO-GUARD PDC-195 DISINFECTANT CONCENTRATE	28.57%
ACME GLY SPRAY	28.46%
GLYCO MIST	28.46%
GAMMA-MENE X-12 HOSPITAL ANTISEPTIC	28%
GLYC-O ZONE	28%
TEXIZE PINE POWER III	27.4%
MINT - AIRE	27.3%
M-CHEM BACTERCIDE NO.4	27.1%
ARCOCIDE B-615 INDUSTRIAL MICROBIOCIDE	26.57%
ALGICIDE 102L	26.4%

PINE POWER II	26%
CAGE CLEANER MINT FRAGRANCE	26%
KURB HC-65	26%
MICROBAN INSTITUTIONAL SPRAY X-580	25%
ISOTHAN DL-1	25%
WITODORANT SPACE DEODORANT	25%
BTC 812	25%
MICROBAN INSTITUTIONAL SPRAY X-580	25%
FYTE 13 HOSPITAL DISINFECTANT	25%
COUGHLAN DE-MOIST MILDEW SPRAY	24.96%
RCI 49-136 GERMICIDE	24.7%
EAGLE RED LABEL GYCOLIZED AROMATIC AIR SANITIZER-DEODORIZER	24.35%
AMWAY DETER SHOE AND SOCK SPRAY	24.35%
AIR DEODORIZER CODE NO. 89-42A	24.3%
CREOLINA	24.25%
JOHNSON END BAC II PRESSURIZED DISINFECTANT SPRAY	24.23%
STRIKE BAC DISINFECTANT PUMP SPRAY	24.01%
BIO-GUARD MDC-175 DISINFECTANT CONCENTRATE	24%
GLYCO-MIST K DEODORIZER-SANITIZER	23.9%
MIDLAND ML DEODORIZER AIR SANITIZER	23.9%
CRYSTALLITE ANTI-BACTERIAL GLASS CLEANER	23%
H-D-10 DISINFECTANT PHENOL COEF 10	22.79%
ZEPREVENT MULTI-PHENOLIC BASED DISINFECTANT	22.74%
FRAGRINE AIR REFRESHER AND AIR SANITIZER	22.5%
WARCOCIDE 1450	22.3%
BLUE ANTISEPT	22.2%
BURNISHINE GERMICIDAL SOLUTION	21%
SANI-JET SPRAY	20.6%
FYTE HOSPITAL GERMICIDAL DETERGENT	20.25%
ALPHA 520	20%
SLIME TROL RX-22	20%
MICROBIOCIDE 250	20%
WATER TREATMENT MICROBIOCIDE WTM-50	20%
NEO-GERM-I-TOL SPECIAL 801	20%
BIOCIDE 286 FOR CONTROL OF BACTERIA AND FUNGI	20%

CERTIFIED NEW GLY-SAN	20%
CERTIFIED'S AIR-SAN AIR SANITIZER DEODORANT SPRAY	20%
H-C NO 479	20%
X-CIDE 17 INDUSTRIAL MICROBIOCIDE	20%
WRICO WMT	20%
WRICO RPV	20%
BARQUAT MC-80	20%
ARQUAD EA 810 (80% CONCENTRATE)	20%
BRENC WATER TREATMENT MICROBIOCIDE	20%
STAFGARD M62 LIQUID GERMICIDAL CONCENTRATE	20%
MOGUL AG-412	20%
GC SUPER 50	20%
METLA COTA ALGAE & SLIME TREATMENT 954	20%
SHARPSAN L-50	20%
SHARPSAN L-50	20%
WATER TREAT 80	20%
CUSTOM-PAK HI-CIDE 210	20%
#800 WATER TREATMENT MICROBIOCIDE	20%
SHILLELAGH 211 MICROBIOCIDE	20%
SUPER WATER TREATMENT MICROBIOCIDE	20%
MANTEK SPRING-AIRE AIR SANITIZER AND DEODORANT	20%
ALPHA 520	20%
SAN DE CLEAN	20%
MICROCIDE MULTI-PURPOSE DISINFECTANT & GERMICIDE AEROSOL	20%
MICROCIDE MULTI-PURPOSE DISINFECT & GERMICIDE LIQUID	20%
BAYCIDE 373	20%
INTEX 8311 STERITEX DETERGENT GERMICIDE	19.8%
CRAIN BREE-ZEE AIR SANITIZER DEODORANT	19.8%
CRAIN MIST AIR SANITIZER-DEODORANT	19.8%
MINTERENE A BROAD SPECTRUM DISINFECTANT WITH MINT-FRESH ODOR	19.46%
CALGON NO. 33 ALGAECIDE	19.4%
CHEM-CLEAN'S PINE ODOR DISINFECTANT	19.4%
RAMELLI BRAND MINT DISINFECTANT	18.83%
FUZZIE BUDDIE SHAMPOO FOR PETS WITH PURE EUCALYPTUS OIL	18.75%
BACTIDINE CONCENTRATE	18.5%

ZEP-O-ZONE SPACE DEODORANT	18.35%
SYNOCIDEN HOSPITAL SPRAY	18.22%
BERGAMOT DISINFECTANT COEF. 6	18%
CAVICIDE	17.2%
CAVICIDE	17.2%
MINTOL XL FRAGRANT MINT DISINFECTANT	16.6%
MISTY MENTHOL SPRAY DECONGESTANT AND AIR SANITIZER	16.05%
MURCO WINTERGREEN DISINFECTANT	16%
CALGO-SAN	16%
MAGNOLIA OLD SPICE AIR SANITIZER GLYCOLIZED SPRAY DEODORANT	15.84%
MINT GLYCOLIZED AIR SANITIZER DEODORIZER	15.8%
SPICE GLYCOLIZED AIR SANITIZER DEODORIZER	15.7%
LEMON GLYCOLIZED AIR SANITIZER DEODRIZER	15.7%
SPEER GLYCOLIZED AIR SANITIZER DEODORIZER	15.7%
EVERGREEN GLYCOLIZED ROOM DEODORANT SPRAY AIR SANITIZER	15.6%
KLEENASEPTIC-B	15.3%
WESTAMINE X CONCENTRATE	15.2%
MIDLAND SYN-O-GERM GERMICIDAL DETERGENT	15%
STAPHICIDE	15%
GERMICIDAL ALL PURPOSE CLEANER CONCENTRATE	15%
MU GERMICIDAL CONCENTRATE	15%
HOSP-ASEPTIC	15%
PINE TREE DISINFECTANT	15%
BACTRON KM-7	15%
ARQUAD EA 810 (50%)	15%
SANICO'S AIR MIST	15%
BIOMET SPRAY SANITIZER	15%
CARGILL Q-DOX 3280	15%
SYN-O-GERM GERMICIDAL DETERGENT	15%
WRICO CRA	15%
ISOTHAN Q-75	15%
FULLER BRUSH GERMICIDAL CLEANER	15%
WRICO CRA	15%
ARQUAD DMCB	15%
BACTRON KM-7	15%

BACTRON KM-7	15%
H-10 MICROBIOCIDE	15%
SANITIZER 256	14.9%
KLEENASEPTIC GERMICIDAL SURFACE CLEANSER FOR NON POROUS SURFACES	14.85%
KLEENASEPTIC GERMICIDAL SURFACE CLEANSER FOR NON POROUS SURFACES	14.85%
BIOMET 7 SANITIZER FOR LAUNDRY RINSES	14.85%
BIOMET 611 DISINFECTANT	14.85%
KLEENASEPTIC GERMICIDAL SURFACE CLEANSER FOR NON POROUS SURFACES	14.85%
TROPIC AIR ROOM DEODORIZER	14.65%
NATIONAL CHEMSEARCH BIO-PHENE	14.5%
ORKIN/AIRE METERED AIR SANITIZER	14.4%
BUTCHER'S GREEN VALLEY	14.2%
BUTCHER'S LEMON TREE	14.2%
BIO-GUARD LDC-165 DISINFECTANT CONCENTRATE	14.1%
H-D-5 DISINFECTANT PHENOL COEF 5	13.61%
NEO-GERM-I-TOL 80%	13.3%
ZEP X 3974	13.25%
PINE DISINFECTANT	13.2%
DUMONT #6 MINT CLEAN DISINFECTANT	13%
PROFESSIONAL GERMICIDAL CONCENTRATE	13%
GERMICIDAL CONCENTRATE	13%
CETYLCIDE	13%
SURGICIDE	13%
DENTICYDE	13%
VAPASEPTIC MINT/SPICE GENUINE GLYCOL AIR SANITIZER	12.85%
SWELL GLYCOLIZER AIR SANITIZER DEODORIZER AND REFRESHENER	12.7%
WRICO MVF	12.6%
VAPASEPTIC	12.56%
WITT-O-SCENT SANITIZER DEODORIZER	12.54%
AIR-GLY	12.54%
ALGEX 30	12.5%
CHEM-SPEC ROOM DEODORANT & AIR SANITIZER	12.35%

MASURY-COLUMBIA HOSPITAL PRODUCT HETRACIDE PHENOLIC GERMICIDE	12.25%
PINEWAY DISINFECTANT CLEANS DEODORIZES	12%
GRIFFIN'S PHEN-ALL 7 CLEANER	12%
SANFAX BACTO-PHENE DISINFECTANT	12%
TERGICIDE K	12%
DYNIDE CONCENTRATED GERMACIDAL DETERGENT	12%
GLYCO MIST DEODORIZER AIR SANITIZER & GERMICIDE AEROSOL	11.95%
CALGN 129 MICRBIOCD F/CTRL BACTERIA-INDUS RECRCULTNG CLNG WTR SYS	11.9%
DI-SPRAY AIR REFRESHENER & SANITIZER	11.7%
PHENOL '8'	11.6%
C-Z AIR - SAN #501	11.58%
BRULIN DISINFECTANT #6	11.1%
AIR GLY-2	11%
BALL-PHENE DISINFECTANT CLEANER	11%
MINT DISINFECTANT DEODORANT, DISINFECTANT, FUNGICIDE, CLEANER	11%
HUNTER'S MAGIC MIST AIR SANITIZER	10.8%
SANI-MINT	10.5%
ESCO MINT	10.5%
WESCODYNE CONC DISIN, GERMICIDAL & FUNGICIDAL CONC DETERGENT	10.5%
WESCODYNE CONCENTRATE	10.5%
PURINA PHENOLIC DISINFECTANT DETERGENT	10%
PURINA GERMICIDE	10%
BRULIN DISINFECTANT CLEANER #14	10%
ANDERSON'S AN-TEC 101 ACID SANITIZER	10%
WASCO ORANGDIS	10%
STERIMINT	10%
GARRATT CALLAHAN FORMULA 35	10%
CHEMSCOPE AIR SANITIZER AND DEODORANT	10%
PELICAN BRAND SANITIZING CLEANER	10%
MINTO	10%
K R C NEW TWINK	10%
CREDO GERMICIDAL CONCENTRATE	10%
SESSCO ALL-IN-ONE	10%

INTEX 8316 PLUS 5	10%
4-D BRAND MINT-CLEANER-DISINFECTANT-SANITIZER	10%
OXFORD SEPTICIDE	10%
DETERG-O-PHENE 1:256 FOR INDUSTRIAL USE ONLY	10%
WRICO KMA	10%
DISINFECTANT GERMICIDAL CONCENTRATE	10%
MINT DISINFECTANT	10%
GERMICIDAL CLEANER	10%
ENVIROMINT MINT ODER DISINFECTANT-DEODORANT	10%
GUARDIAN STERI-A-MEN 7000	10%
LAVENDAR AIR SANITIZER AND DEODORIZER	10%
BUCKINGHAM MINT DISINFECTANT	10%
ROCKFORD NO 1430 ACID SANIT	10%
TOP-SAN	10%
METASOL CP	10%
CONTROL FLUID FOR BIG STINKY FLY TRAP	10%
SANITIZED HBF	10%
SANITIZED 255	10%
PHENOLIC DISINFECTANT	10%
SANI KLEEN	10%
STAR MAID SANI KLEEN	10%
FORMULA 76 DISINFECTANT-CLEANER-SANITIZER-FUNGICIDE-DEODORANT	10%
LIQUID DETERGENT SANITIZER	10%
WASCO LILADIS	10%
VESPRAY	9.92%
MC-301 MICROBIOCIDE AND DEPOSIT INHIBITOR	9.9%
UNITED SANITIZED HOUSEHOLD SPRAY	9.55%
REXALL REFRESH AIR SPRING BOUQUET	9.55%
REXALL REFRESH AIR PINE FOREST	9.55%
PINOX 13	9.5%
SANI-PINE DISINFECTANT DEODORANT CLEANER	9.5%
PURE PINE ODOR 13 QUATERMARY DISINFECTANT	9.5%
SANO-PINE ODOR DISINFECTANT DEOD.	9.5%
POLY PINE FRAGANCE GERMICIDAL CLEANER, COEFFICIENT 13	9.5%
PINE SCENT DEODORANT-DISINFECTANT	9.5%

BLAINE PINE ODOR 13 DISINFECTANT	9.5%
PINE-SOL	9.5%
ROMAN PINE ODOR 13	9.5%
WINSTON PINE ODOR DISINFECTANT COEF.13	9.5%
ALLSTATES CHEMICAL PINE SCENT 13DISINF.DEOD.	9.5%
SANCO PINE ODOR 13 DISINF. DET. SANITIZER DEODARIZER	9.5%
HALE'S PINE ODOR 13 DISINFECTANT CLEANER DEODORANT	9.5%
JAN-MASTER SUPER PINE ODOR DISINFECTANT DEODORANT	9.5%
SOFT PINE "13"	9.5%
PINOX 13	9.5%
PINOX 13	9.5%
PINE AWAY 13 PINE ODOR DISINFECTANT	9.5%
BEAVER PINE ODOR 13 DISINFECTANT	9.5%
LEONARD'S PINE ODOR 13 DISINFECTANT CLEANER	9.5%
CLAYTON'S PINE ODOR DISINFECTANT CONCENTRATE	9.5%
CHEM GUARD GERMICIDAL CLEANER PINE ODOR 13	9.5%
PINE ODOR P-1513	9.5%
PINE CLEAN-UP PINE ODOR DISIN.COEF.13	9.5%
MICRO-PINE PINE ODOR DISINFECTANT COEF.13	9.5%
LEMON DISINFECTANT CONCENTRATE BASE	9.3%
LEMON DISINFECTANT CONCENTRATE BASE	9.3%
(NEW) RAMO MINT AIR SANITIZER AND ROOM DEODORANT	9.3%
STERI-SCENT FOR REFRIGERATORS SURFACE DEODORANT	9.3%
BUTCHER'S PROBE GERMICIDAL DETERGENT	9.29%
BURNISHINE DISINFECTANT SOLUTION & PUMP SPRAY	9.2%
SCOTCH HEATHER	9%
NALCON 243 MICROORGANISM CONTROL CHEMICAL	9%
ORB GLYCOL TYPE AIR SANITIZER AEROSOL DEODORANT	8.95%
ASEPTIPHENE	8.83%
A-CHLOROPHENYL	8.75%
CLENESCO ARC	8.5%
DETERGENT DISINFECTANT DEODORANT SANITIZER PINE ODOR	8.04%
MICROBIOCIDE 220	8%
COMMANDO PINE-O-CIDE-10 DISINFECTANT	8%
SANI-CLOTH GERMICIDAL DISPOSABLE CLOTH	8%

CALUSA MILDEW PREVENTIVE	8%
BURNISHINE GERMICIDAL CLOTH	8%
OWT-200 MICROBIOCIDE	8%
LEMON SCENTED DISINFECTANT COEF. 5	8%
DIAMOND DISINFECTANT DETERGENT&DEODORIZER WINTERGREEN ODOR	7.95%
SO-CLEAN FOAMING CLEANSER	7.85%
CONCENTRATED AIR SANITIZER AND DEODORIZER	7.8%
SANATROL DISINFECTANT	7.5%
NURSES AID HOSPITAL DISINFECTANT	7.4%
M2 CLEANER AND DEODORANT	7%
TEXIZE 8255 A BATHROOM CLEANER	7%
TEXIZE FIBERGLASS PLUS DISINFECTANT BATHROOM CLEANER	7%
MCNESS BACTERIOSTATIC DUST MOP SPRAY	7%
FANTASTIK BATHROOM CLEANER	7%
BAC STOP BACTERIOSTATIC DUST CLOTH/DUST MOP SPRAY	7%
A-108 MICROBIOCIDE	6.67%
LEMON DISINFECTANT CONCENTRATE DEODORANT CLEANER	6.55%
DI-CHEM 650 BACTERICIDE	6.5%
BIOMET 3 ANTIMICROBIAL COMPOUND	6.5%
BIO GUARD M-25 DISINFECTANT	6.25%
BIO GUARD BTM CONCENTRATE	6.14%
CRESOL,BLACK DISINFECTANT	6%
BIG D AIR SANITIZER AND DEODORANT	6%
SOFTPINE DISINFECTANT CLEANSER DEODORANT	6%
BIOSPERSE 214	6%
SOFTPINE DISINFECTANT CLEANSER DEODORANT	6%
SO/SAN 30 CONCENTRATED SOFTENER SANITIZER FOR MANUFACTURING USE ONLY	6%
SOFT-O-PINE	6%
BIO GUARD QP-5 PINE ODOR CLEANSER DISINFECTANT DEODORANT	6%
BARRIER DET BACTERIOSTAT SUPER CONC FED SPEC P=001397 (GSA-FSS)	5.8%
MILDUPRUF	5.75%
MILDUPRUF	5.75%
MILDUPRUF	5.75%
PHENICIDE A	5.62%

PINE ODOR DISINFECTANT	5.6%
BREATH OF SPRING ROOM DEODORANT AND SANITIZER	5.25%
SPRING GARDEN ROOM DEODORANT AND SANITIZER	5.25%
BETZ SLIME TROL RX38	5%
FORMULA 67-6 SANITIZER AND CLEANER	5%
SUDIA WAR-PHENE	5%
OLIN ALGICIDE "G"	5%
LC 100 IODOPHOR	5%
IOQUAT	5%
SANITREET BACTERIOSTATIC DUST ABSORBER MIST	5%
LILA-PHENE	5%
FORMULA 67-6 SANITIZER AND CLEANER	5%
ACCO TRIPHENE	5%
NEO-GERM-I-TOL 50%	5%
20 MULE POWER BATHROOM CLEANER	5%
20 MULE POWER SHOWER TUB & TILE CLEANER	5%
OLIN ALGICIDE "G"	5%
GRIFFIN'S HYPINE 8 DISINFECTANT	5%
OXFORD KONTROL COOLING TOWER SLIMICIDE	5%
PACE TERGICIDE G GERMICIDE AND DETERGENT	5%
BACTIN LIQUID BACTERIOSTAT-SANITIZER	5%
BIO GUARD LAUNDRI-STAT T-522	5%
BIO-GUARD M-20 DISINFECTANT	5%
LIQUID SANI FLUFF WITH NOXGERM	5%
VINELAND HI LETHOL 50 DISINFECTANT CONCENTRATE	5%
BIO QUAT 50-30	5%
BUTCHERS ALPINE AIR SANITIZER	5%
BLAINE LEMON DISINFECTANT CONCENTRATE	5%
LEMOPHENE	5%
ALGAECIDE-QA	5%
PINE-O-LINE PINE ODOR DISINFECTANT	5%
SPIES HOSPITAL DISINFECTANT	5%
CHEM-GUARD LEMON DISINFECTANT CONC.	5%
DYCHO IODINE UDDER WASH	5%
PURINA I-Q GERMICIDE	5%

C-13 CONCENTRATED CLEANER & DISINFECTANT	5%
PHENOLA DETERGENT-GERMICIDE	4.78%
PINOX 6	4.75%
PINE ODOR 6 DISINFECTANT	4.75%
SANI=CHEM PINE ODOR DISINFECTANT	4.75%
BEAVER PINE ODOR 6 DISINFECTANT	4.75%
PINE ODOR DISINFECTANT	4.75%
SANI-PINE PINE ODOR DISINFECTANT COEF.6	4.75%
ROMAN PINE ODOR 6	4.75%
WINSTON PINE ODOR DISINFECTANT COEF. 6	4.75%
ALLSTATES CHEMICAL PINE SCENT DISINFFECTANT-DEODORANT	4.75%
SANCO PINE ODOR 6 DISINFECTANT	4.75%
HALE S PINE ODOR 6 DISINFECTANT CLEANER DEODORANT	4.75%
CHEMPINE DISINFECTANT AND DEODORANT	4.75%
ACCO PINE ODOR DISINFECTANT COEF.6	4.75%
TEX-O-PINE	4.75%
PROCHEM PINE ORDOR DISINFECTANT COEF. 6	4.75%
PINE ODOR SANAMAX P6	4.75%
ALLSTATES CHEMICAL PINE SCENT DISINFFECTANT-DEODORANT	4.75%
MERCO PINE ODOR DISINFECTANT PHENOL COEF.6	4.75%
PINOX 6	4.75%
PINOX 6	4.75%
CHEMEX PINE ODOR DISINFECTANT	4.75%
PINE AWAY 6 PINE ODOR DISINFECTANT	4.75%
SOLVENTOL 8505 CLEANER DISINF	4.75%
PINO CLEAN DISINFECTANT DEODORANT CLEANER	4.75%
PURE PINE ODOR 6	4.75%
STERLING PINE ODOR DISINFECTANT	4.75%
BIG K PINE ODOR DISINFECTANT	4.75%
POLY PINE FRAGRANCE GERMICIDAL CLEANER COEFFICIENT 6	4.75%
PINE ODOR DISINFECTANT	4.75%
PINE TREE ODOR DISINFECTANT	4.75%
NEEDLE PINE ODOR DISINFECTANT	4.75%
PINE ODOR DISINF CLEANER DEOD	4.75%
2M PINE ODOR DISINFECTANT-CLEANER COEF.6	4.75%

VIKING HARVEST PINE ODOR DISINFECTANT	4.75%
LEONARD'S PINE ODOR 6 DISINFECTANT CLEANER	4.75%
CHEM GUARD GERMICIDAL CLEANER PINE ODOR 6	4.75%
P-76 PINE ODOR	4.75%
WILLO PINE PINE ODOR DISINFECTANT	4.75%
MICRO-PINE PINE ODOR DISINFECTANT COEF.6	4.75%
STERI-AMPS CONCENTRATED GERMICIDE 10%	4.7%
ACCO-ALGICIDE 10-01	4.5%
LIEN 822 SANITIZER	4.25%
NEW LF-10 HOSPITAL DISINFECTANT CONCENTRATE	4.2%
TEXIZE 4055 BATHROOM CLEANER	4.1%
OZARK BAXAN	4%
ROMAN MINT 15 DISINFECTANT	4%
SPEEDEE-1000	4%
ALLSTATES MINT FRAGARANCE 15 DISINFECTANT-DEODORANT	4%
OWT-100 MICROBIOCIDE	4%
SANCO MINT ODOR 15 DISINFECTANT SANITIZER DEODORIZER	4%
HALE MINT ODOR 15 DISINFECTANT CLEANER DEODORANT	4%
OZARK BAXAN	4%
JAN-MASTER SUPER MINT DISINFECTANT DEODORANT	4%
CIGOMENT DISINFECTANT	4%
CHEM-GUARD GERMICIDAL CLEANER MINT ODOR 15	4%
CLAYTON'S MINT DISINFECTANT CONCENTRATE	4%
WILLIS MINT DISINFECTANT CONCENTRATE	4%
MINT CLEAN UP MINT ODOR DISINFECTANT COEF. 5	4%
MINT O MINT CLEANSER DISINFECTANT DEODORANT	4%
NAPASCO MINT 44 DETERGENT DISINFECTANT	4%
NAPASCO MINT 44 DETERGENT DISINFECTANT	4%
PEP O MINT 15 DISINFECTANT DETER SANITIZER DEO.	4%
MINT POWER DISINFECTANT DEODORANT CLEANER	4%
PURE MINT ODOR 15	4%
PEP O MINT 15 DISINFECTANT DETER SANITIZER DEO.	4%
POLY MINT FRAGANCE GERMICIDAL CLEANER COEFFICIENT 15	4%
BACTRON K-22	4%
PREMIER NO. 150 MICROBIOCIDE	4%

BLAINE MINT DISINFECTANT CONCENTRATE	4%
HANCO 970 MINT DISINFECTANT	4%
MINT FRAGRANT DISINFECTANT	4%
C&B MINT 15 DISINFECTANT	4%
VAPORENE FX-80 MICROBICIDE	4%
FREMONT 9015 MICROBIOCIDE	4%
MINT-SOL 15	4%
MINT-SOL	4%
MICRO-ORANGE 15 DETERGENT DISINFECTANT	4%
MICRO MINT 15 DETERGENT DISINFECTANT	4%
MICROBIOCIDE 210	4%
NAPASCO MINT 44 DETERGENT DISINFECTANT	4%
GERMICIDAL NEUTRO JEL	4%
BIOMET 600 CONCENTRATE	3.98%
WYANDOTTE PREVIEW PLUS PHENOLIC GERMICIDAL DETERGENT	3.97%
FORMULA 4029	3.6%
MOLAR "O.S.T."	3.6%
GC 20 HEAVY DUTY GERMICIDE	3.6%
LADRIN HDG	3.6%
JERMI-KLEEN	3.6%
SANITEX	3.6%
SPEEDGE 4.5	3.6%
BIO-GUARD L-25 DISINFECTANT	3.53%
WINDEX ANTIBACTERIAL GLASS & SURFACE CLEANER	3.5%
TEXIZE NEW 5825 PINE ODOR DISINFECTANT CLEANER	3.5%
TEXIZE NEW 5822 DISINFECTANT CLEANER	3.5%
FRESH LEMON DISINFECTANT	3.3%
KENNEL GUARD DISINFECTANT DEODORIZER CONCENTRATE	3.3%
LEMON DISINFECTANT NO. 20 CLEANER DISINFECTANT DEODORIZER	3.1%
LEMON DISINFECTANT NO. 20 CLEANER DISINFECTANT DEODORIZER	3.1%
MINT DISINFECTANT	3.05%
OZARK BIOTOL	3%
GUARDIAN HIGHLY CONCENTRATED GERMICIDE	3%
FORMULA-56 SANITIZER	3%
TEXIZE LEMON POWER DISINFECTANT GERMICIDE	3%

BARCOLENE'S PINE SCENT DISINFECTANT COEF. 2.5	3%
MAYFAIR SUPER COUNT DOWN	3%
DICAL	3%
GERMICICDAL DETERGENT	3%
FREE'N' CLEAR CONCENTRATED DISINFECTANT	3%
CHEM-CLEAN'S GERM-X	3%
TEK H-600	3%
FC 505 GERMICIDAL CLEANER	3%
TC 505 ORANGE DISINFECTANT	3%
GC SUPER 40	3%
DOUBLE-D	3%
LADRIN CLEAN-SAN	3%
ULTRA-SAN CONCENTRATE	3%
INTEX 8065 PRIME DISINFECTANT CLEANER	3%
LICO 30 HIGHLY CONCENTRATED GERMICIDE	3%
GERMICIDAL CLEANER HOSPITAL STRENGTH	3%
OZARK BIOTOL	3%
HALF OUNCE	3%
EXCEL X-256	3%
FORMULA 4027	3%
CCC DISINFECTANT SANITIZER FUNGICIDE DEODORIZER	3%
K.O.-100	3%
SUPER STERISOL DISINFECTANT	3%
MOLAR HI-CQ	3%
INTEX DOUBLE FEATURE DISINFECTANT CLEANER	3%
QRL SANI-GERM	3%
LUCKY PINE,DISINFECTANT CLEANSER	3%
FLEXO FORMULATION 35-6	3%
NET-DIP DISINFECTANT-SANITIZER FUNGICIDE-DEODORIZER	3%
PURITAN #5566	3%
WASCO MINTKLEAN II	3%
BIO-GUARD L-20 DISINFECTANT	2.82%
EDCO-SYN	2.78%
TRU-KLEEN INSTITUTIONAL HD DEODARANT DISINFECTANT CLEANER	2.6%
TRU-KLEEN INSTITUTIONAL HD DEODARANT DISINFECTANT CLEANER	2.6%

ACCO 9-11-M	2.5%
SC 710 ALGAECIDE	2.5%
BIO GUARD M-10 DISINFECTANT	2.5%
ALCORIN AMC	2.5%
ACCO 9-11-M	2.5%
BETA-PHENE 128	2.5%
SANITIZER FABRIC SOFTENER CONCENTRATE	2.5%
SSS 128 PHENOLIC GERMICIDAL DETERGENT	2.5%
DETERGENT-BACTERIOSTAT GENERAL PURPOSE SUPER CONCENTRATE	2.5%
ACORN BRAND HY-POWER CLEANER-SANITIZER-DISINFECTANT	2.5%
SUPER PHENOLA DETERGENT-GERMICIDE	2.5%
BLUE RIBBON UDDER WASH AND SANITIZER	2.4%
STERAZONE DAIRY ONLY	2.4%
CLIPPER MATE, LUBRICATES SANITIZES COOLS	2.4%
DAIRY DEW STERAGENT UDDER WASH AND SANITIZER	2.4%
MILKHOUSE BRAND STERAMINE MARK I	2.4%
LF-10 HOSPITAL DISINFECTANT CONCENTRATE	2.38%
BIO-GUARD SL-5 DISINFECTANT, CLEANSER DEODORANT	2.35%
SANI-LEMON DISINFECTANT CLEANSER DEODORANT	2.35%
DISINFECTANT NO. 918	2%
ROMAN LEMON 15 DISINFECTANT	2%
ROMAN MINT 7 DISINFECTANT	2%
WINSTON LEMON ODOR DISINFECTANT COEF. 15	2%
ALLSTATES LEMON SCENT 15 DISINFECTANT-DEODORANT	2%
ALL STATES MINT FRAGRANCE DISINFECTANT	2%
CHEMEX LEMON ODOR DISINFECTANT	2%
SANCO MINT ODOR 7 DISINFECTANT	2%
SANCO LEMON ODOR 15 DISINFECTANT DET. SANITIZER DEO.	2%
BEAVER LEMON ODOR 15 DISINFECTANT	2%
LEONARD'S MINT ODOR 7 DISINFECTANT CLEANER	2%
CHEM-GUARD GERMICIDAL CLEANER MINT ODOR 7	2%
CHEM-GUARD GERMICIDAL CLEANER LEMON ODOR 15	2%
CLAYTON'S LEMON ODOR DISINFECTANT CONCENTRATE	2%
CENTER FRESH MINT 7 DISINFECTANT	2%
WILLIS LEMON DISINFECTANT CONCENTRATE-COEF 15	2%

MINT M-107	2%
LEMON L-2015 DISINF., DETER., SANIT., DEOD.	2%
MINT 7 DISINFECTANT DEODRIZER CLEANER	2%
COLLEGE MINT 7 DISINFECTANT	2%
TUFF MINT 7 DISINFECTANT	2%
INTENSIVE CARE	2%
STRATACIDE	2%
CHIN HILLS PINK STUFF	2%
LEMON CLEAN-UP LEMON ODOR DISINFECTANT COEF. 15	2%
CONQUEST	2%
AERO-PHEEN	2%
HANCO 980 LEMON DISINFECTANT	2%
LEMON SCENT DISINFECTANT	2%
MINT ODOR DISINFECTANT	2%
HALE'S LEMON ODOR 15 DISINFECTANT	2%
HALE S MINT ODOR 7 DISINFECTANT	2%
MAINLINE WINTERGREEN 7 DISINFECTANT DEODORANT	2%
T.I.C. LEMON 15 DISINFECTANT, CLEANER DEODORANT	2%
PROCHEM MINT ODOR DISINFECTANT COEF. 7	2%
2M MINT ODOR DISINFECTANT-CLEANER COEF. 7	2%
MINT ODOR DISINFECTANT	2%
CHEMCON MINT 7 DISINFECTANT, CLEANER, DEODORANT	2%
VIKING JULEP MINT FRAGRANCE DISINFECTANT CLEANER DEODORIZER	2%
SANAMAX M7	2%
NEW OZON-O-PHENE	2%
SANI-QUAT CENTURY DISINFECTANT & SANITZER NO.2017	2%
CENTURY NO. 3024 MINT DISINFECTANT-CLEANER	2%
ALL STATES MINT FRAGRANCE DISINFECTANT	2%
MERCO MINT ODOR DISINFECTANT	2%
DEARCIDE 706	2%
PEP O MINT 7 DISINFECTANT DETER. SANITIZER DEO.	2%
LEMON X 15 DISINFECTANT DETERGENT SANITIZER DEODORIZER	2%
MINTY DISINFECTANT DEODORANT CLEANER	2%
PURE LEMON ODOR IS QUATERNARY DISIN.-DET.-DEOD.-SANIT.	2%
STERLING MINT ODOR DISINFECTANT	2%

KLENZTONE MINT 7 DISINFECTANT CLEANER	2%
POLY LEMON FRAGRANCE GERMICIDAL CLEANER COEF. 12	2%
POLY LEMON FRAGRANCE GERMICIDAL CLEANER 15	2%
POLY ORANGE FRAGRANCE 12	2%
MOSAN - CDD	2%
BLAINE LEMON CONC. COEF. 15	2%
NAPASCO MINT FRAGRANT-22	2%
DISINFECTANT NO. 918	2%
NAPASCO MINT FRAGRANT-22	2%
BIO-GUARD MP-22	2%
8506 CLEANER DISINFECTANT	2%
HEAVY DUTY LEMO-SAN DISINFECTANT DEODORANT CLEANER	2%
LEMO CLEAN DIS DISINFECTANT CLEANER DEODORANT	2%
MINT-SOL 7 DISINFECTANT-SANITIZER DEODORIZER-DETERGENT	2%
CITRU-SOL 15 DISINFECTANT CLEANER DEODORANT	2%
CITRU-SOL	2%
MOM'S MINT DISINFECTANT	2%
MINT FRAGRANCE DISINFECTANT	2%
MICRO-MINT 7 DETERGENT DISINFECTANT	2%
MICRO-ORANGE 22 DETERGENT DISINFECTANT	2%
MICRO-MINT 22 DETERGENT-DISINFECTANT	2%
MICRO-LEMON ODOR DETERGENT-DISINFECTANT COEF.15	2%
MICRO-ORANGE DISINFECTANT DETERGENT	2%
MINTOLENE	2%
MINT CDD CLEANER DEODORIZER DISINFECTANT	2%
UNITED UCO MINT DISINFECTANT	2%
MINT ODOR COEF-5	1.98%
GP-23 GLAD CLEAN	1.96%
SANSPRAE	1.92%
LEMON ODOR GERMICIDAL CLEANER DISINFECTANT DEODORANT COEF. 10	1.9%
ANTISEPTOL G/C	1.78%
GUARDALL DISINFECTANT AND RESIDUAL BACTERIOSTAT	1.65%
POLY LEMON FRAGRANCE 10	1.6%
LEMON GERMICIDE & DEODORIZER	1.6%
LEMONIZE	1.55%

LEMON DISINFECTANT NO. 10 DISINFECTANT-DEODORIZER-CLEANER	1.55%
BIO-GUARD 452 HATCHERY DETERGENT-SANITIZER	1.55%
CLIC GERMICIDAL CLEANER	1.5%
SAN-SOFT CONCENTRATE	1.5%
BIO-GUARD L-10 DISINFECTANT	1.41%
HUNTINGTON GERMICIDAL CLEANER	1.32%
HUNTINGTON 256 GERMICIDAL DETERGENT	1.2%
SPECIAL CLEANER #1	1.2%
STANHOME GERM-TROL DISINFECTANT DEODORANT GERMICIDE	1.03%
LEMON CDD CLEANER-DEODORIZER-DISINFECTANT	1%
NEO-GERM-I-TOL 10%	1%
DEMERT DAISY FRESH DISINFECTANT CLEANER	1%
STIFLE	1%
HALE'S LEMON ODOR 7 DISINFECTANT	1%
CHEMA LEMON DISINFECTANT AND DEODORANT	1%
MAINLINE LEMON ODOR 7 DISINFECTANT DEODORANT FOR HOSPITAL USE	1%
T.I.C. LEMON 7 DISINFECTANT CLEANER DEODORANT	1%
SUNSHINE LEMONENE DISINFECTANT-CLEANER	1%
SUNSHINE LEMONENE DISINFECTANT-CLEANER	1%
CHEMCON LEMON 7 DISINFECTANT, CLEANER, DEODORANT	1%
BEAVER LEMON ODOR 7 DISINFECTANT	1%
CHEM GUARD GERMICIDAL-CLEANER LEMON ODOR 7	1%
WILLIS LEMON DISINFECTANT CONCENTRATE COEF. 7	1%
LEMON L-107	1%
SANI CENT LEMON ODOR DISINFECTANT	1%
LEMON X 7 DISINFECTANT DETERGENT SANITIZER DEO.	1%
SOLVENTOL 8504 CLEANER DISINFECTANT	1%
LEMO SAN DISINFECTANT DEODORANT CLEANER	1%
POLY LEMON FRAGRANCE GERMICIDAL CLEANER 7	1%
LEMON ODOR GERMICIDAL CLEANER DISINFECTANT DEODORANT COEF. 5	1%
BLAINE LEMON DISINFECTANT CONC. COEF. 7	1%
LEMON SCENT DISINFECTANT	1%
ROMAN LEMON 7	1%
SANCO LEMON ODOR 7 DISINFECTANT	1%
STIFLE	1%

TARGOSZ GERMICIDE PLUS	1%
MICRO-LEMON 7 DETERGENT DISINFECTANT	1%
INTEX 8312 GERMICIDAL DETERGENT	.88%
DUST TEX TREATING FLUID ADDITIVE P-6	.87%
FULLPHENE II	.87%
SHAVA LUBE	.82%
POLY LEMON FRAGRANCE 5	.8%
CONCENTRATE GRE-SOLV GERMICIDAL CLEANER	.75%
RITE BRAND LEMON ODOR CLEANER	.5%
ASEPTICARE CONTACT DISINFECTANT ODOR COUNTERACTANT SPRAY	.43%
CHEMTECH DISINFECTANT DEODORANT SPRAY NO. 11	.43%
CHEMTECH DISINFECTANT DEODORANT SPRAY	.43%
CHEMTECH DISINFECTANT DEODORANT SPRAY NO. 14	.43%
CHEMTECH DISINFECTANT DEODORANT SPRAY	.43%
CHEMTECH DISINFECTANT DEODORANT SPRAY NO. 9	.43%
PINE ASEPTICARE	.43%
CHEMTECH DISINFECTANT DEODORANT SPRAY #13	.41%
MAL-D-MER	.27%
VOBAN	.27%
EME STAT	.27%
DEL ADIOS	.27%
COLUMBIA PINE OIL DISINFECTANT	.15%
B&T COMPOUND 701	.11%
BIOMET 630 DISINFECTANT AND FOR FOGGING APPLICATIONS	.11%
DISINFECTANT, GERMICIDAL AND FUNGICIDAL CONCENTRATE O-D-406 TYPE L	.1%
CETYLITE SPRAY CLEANER	.09%
SANI-SEPTO BOWL CLEANER CONCENTRATE	.06%
SANITANE BACTERIOSTATIC DUST CONTROLLER	.06%
ONE STROKE BACTERIOSTATIC DUST CONTROLLER	.06%
ALLERGEN MIST	.03%
WITT O LITE BACTERIOSTATIC DUST TREATMENT	.03%
RANCH GARD FORMULA 'R' GERMICIDE-FUNGICIDE	.03%

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Regulatory Coverage

of ISOPROPYL ALCOHOL (67-63-0) from Scorecard

Federal Regulatory Program Lists

- Air Contaminants (Occupational and Safety Health Act)
- Registered Pesticides (Federal Insecticide, Fungicide, and Rodenticide Act)
- Toxic Release Inventory Chemicals

California State Regulatory Program Lists

- California Air Toxics "Hot Spots" Chemicals (Assembly Bill 2588)

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Basic Testing to Identify Chemical Hazards

for ISOPROPYL ALCOHOL (67-63-0) from Scorecard

The U.S. EPA conducted a comprehensive review of publicly available chemical testing data in 1997 to examine whether the basic information needed to identify chemical hazards is available for high production volume chemicals. EPA searched major chemical databases to determine if the following tests had been conducted on a chemical:

- Acute toxicity
- Chronic toxicity
- Neurotoxicity
- Developmental or reproductive toxicity
- Mutagenicity
- Carcinogenicity
- Ecotoxicity
- Environmental fate

Eight basic tests to identify chemical hazards have been conducted and are publicly available for this chemical.

More on the importance of basic toxicity testing

Reference

EPA. Chemical Hazard Data Availability Study: High Production Volume (HPV) Chemicals and SIDS Testing
Office of Pollution Prevention and Toxics, EPA,Washington, DC. 1998.

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Safety Assessment Data

for ISOPROPYL ALCOHOL (67-63-0) from Scorecard

Are Risk Assessment Values Available?

Health Risk of Concern	Inhalation	Ingestion
Cancer	Not a recognized carcinogen	Not a recognized carcinogen
Noncancer	**No**	**No**

Are Exposure Data Available?

Type of Exposure	
Inhalation - ambient air	**No**
Inhalation - indoor air	**No**
Ingestion	**No**

- See the data US EPA possesses for safety assessment.

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Scorecard Risk Characterization Data

for ISOPROPYL ALCOHOL (67-63-0) from Scorecard

Risk Assessment Values or Standards

	Value	Units	Reference
Inhalation cancer risk value (potency)	Not a recognized or suspect carcinogen		
Inhalation noncancer risk value (reference concentration)	7000	ug/m3	OEHHA2000-REL
National ambient air quality standard	Gap in regulatory coverage		
Ingestion cancer risk value (potency)	Not a recognized or suspect carcinogen		
Ingestion noncancer risk value (reference dose)	Data gap		
National water quality standard	Gap in regulatory coverage		

See the data US EPA possesses for safety assessment.

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ISOPROPYL ALCOHOL

CAS Registry Number: 67-63-0

Structure: $CH_3CHOHCH_3$

Molecular Formula: C_3H_8O

Description

Isopropyl alcohol is a volatile, flammable, clear, colorless liquid which has a slight odor resembling that of a mixture of ethanol and acetone. It has a bitter taste. Although miscible with water, other alcohols, ether, and chloroform, it is insoluble in salt solutions (Merck, 1989).

Physical Properties of Isopropyl alcohol

Molecular Weight	60.09
Boiling Point	82.5 oC
Melting Point	-88.5 oC
Flash Point	11.7 oC (53 oF) (closed cup)
Vapor Pressure	44 mm Hg at 25 oC
Density/Specific Gravity	0.7851 at 20/4 oC (water = 1)
Log/Octanol Water Partition Coefficient	0.05
Dissociation Constants	pka: 17.1 at 25 oC
Autoignition Temp	455.6 oC (852 oF)
Henry's Law Constant	8.07 x 10-6 atm-m3/mole
Vapor Density	2.08 (air = 1)
Conversion Factor	1 ppm = 2.45 mg/m3

(HSDB, 1991)

SOURCES AND EMISSIONS

A. Sources

Isopropyl alcohol is used in the manufacture of acetone, glycerol, isopropyl acetate, shellacs, quick drying inks, and creosote. It is a solvent for essential and other oils, alkaloids, gums, resins, coatings and cellulose, and a deicing agent for liquid fuels, lacquers, and extraction processes. It is also used in antifreeze compositions and as an antiseptic (Sax, 1987; Howard, 1990; Merck, 1989).

Isopropyl alcohol is registered as an antimicrobial, bactericide, fungicide, and virucide. It is used for

sterilizing and disinfecting surfaces in hospitals, dairy farms, food processing plants, eating establishments, and in household dwellings. Isopropyl alcohol is also registered for use as a topical disinfectant in animal areas in and around the house, in veterinary institutions, farm structures, poultry areas, and in hatcheries and zoo animal premises. It is registered for use in barbershops for cleaning hair cutting and styling instruments and equipment. Isopropyl alcohol is also registered as an adjuvant, used to facilitate pesticide applications in agricultural settings, and as an adjuvant in industrial water washer, cooler, and condenser systems (DPR, 1996).

The licensing and regulation of pesticides for sale and use in California are the responsibility of the Department of Pesticide Regulation (DPR). Information presented in this fact sheet regarding the permitted pesticidal uses of isopropyl alcohol has been collected from pesticide labels registered for use in California and from DPR's pesticide databases. This information reflects pesticide use and permitted uses in California as of October 15, 1996. For further information regarding the pesticidal uses of this compound, please contact the Pesticide Registration Branch of DPR (DPR, 1996).

The primary stationary sources that have reported emissions of isopropyl alcohol in California are the leather tanning and finishing industry, manufacture of miscellaneous food and kindred products, and commercial printing facilities (ARB, 1997b).

B. Emissions

Emissions can be generated from petroleum storage, auto exhaust, plastics combustion, printing, sewage treatment, wood pulping, as well as consumer products (Howard, 1990). The total emissions of isopropyl alcohol from stationary sources in California are estimated to be at least 310,000 pounds per year, based on data reported under the Air Toxics "Hot Spots" Program (AB 2588) (ARB, 1997b).

C. Natural Occurrence

Isopropyl alcohol occurs as a plant volatile and has been found in animal waste and microbes (Howard, 1990).

AMBIENT CONCENTRATIONS

No Air Resources Board data exist for ambient measurements of isopropyl alcohol.

INDOOR SOURCES AND CONCENTRATIONS

Isopropyl alcohol is a component of many antiseptic and cosmetic products used indoors. No information about indoor concentrations of isopropyl alcohol was found in the readily-available literature.

ATMOSPHERIC PERSISTENCE

Isopropyl alcohol exists in the atmosphere in the gas phase. The dominant atmospheric loss process for isopropyl alcohol in the troposphere is by reaction with the hydroxyl radical. Based on this reaction, the

atmospheric half-life and lifetime of isopropyl alcohol is estimated to be 1.9 days and 2.7 days, respectively (Atkinson, 1994). The major reaction product from this reaction is acetone (Atkinson, 1995).

AB 2588 RISK ASSESSMENT INFORMATION

Although isopropyl alcohol is reported as being emitted in California from stationary sources no health values (cancer or non-cancer) are listed in the California Air Pollution Control Officers Association Air Toxics "Hot Spots" Program Revised 1992 Risk Assessment Guidelines for use in risk assessments (CAPCOA, 1993).

HEALTH EFFECTS

Probable routes of human exposure to isopropyl alcohol are inhalation and ingestion.

Non-Cancer: Isopropyl alcohol vapors are mildly irritating to the eyes and upper respiratory tract. At high levels, isopropyl alcohol can cause central nervous system (CNS) depression. Symptoms of poisoning include dizziness, incoordination, headache, and confusion. Isopropyl alcohol is metabolized to acetone which may prolong or potentiate the CNS depression. Isopropyl alcohol may enhance the hepatotoxicity of carbon tetrachloride (Olson, 1994).

The United States Environmental Protection Agency (U.S. EPA) has not established a Reference Concentration (RfC) or an oral Reference Dose (RfD) for isopropyl alcohol (U.S. EPA, 1995a).

Limited information is available on the reproductive toxicity of isopropyl alcohol. In the rat, high maternally-toxic inhalation exposures were associated with reduced fetal weight and increased skeletal and visceral malformations (HSDB, 1995).

Cancer: The U.S. EPA has not classified isopropyl alcohol as to its carcinogenic potential (U.S. EPA, 1995a). The International Agency for Research on Cancer has classified isopropyl alcohol in Group 3: Not classifiable as to its carcinogenic potential (IARC, 1987a).

International Chemical Safety Cards

ISOPROPYL ALCOHOL

ICSC: 0554

ISOPROPYL ALCOHOL
2-propanol
Isopropanol
$C_3H_8O/(CH_3)_2CHOH$
Molecular mass: 60.1

CAS # 67-63-0
RTECS # NT8050000
ICSC # 0554
UN # 1219
EC # 603-003-00-0



TYPES OF HAZARD/ EXPOSURE	ACUTE HAZARDS/ SYMPTOMS	PREVENTION	FIRST AID/ FIRE FIGHTING
FIRE	Highly flammable. Heating will cause rise in pressure with risk of bursting.	NO open flames, NO sparks, and NO smoking.	Powder, alcohol-resistant foam, water in large amounts, carbon dioxide.
EXPLOSION	Vapour/air mixtures are explosive.	Closed system, ventilation, explosion-proof electrical equipment and lighting.	In case of fire: keep drums, etc., cool by spraying with water.
EXPOSURE			
• **INHALATION**	Cough. Dizziness. Drowsiness. Headache. Nausea. Sore throat. Vomiting.	Ventilation, local exhaust, or breathing protection.	Fresh air, rest. Refer for medical attention.
• **SKIN**	Redness.	Protective gloves.	Remove contaminated clothes. Rinse skin with water.
• **EYES**	Redness. Pain. Blurred vision.	Safety goggles.	First rinse with plenty of water for several minutes (remove contact lenses if easily possible), then take to a doctor.
• **INGESTION**	Dizziness. Drowsiness. Nausea. Sore throat. Vomiting.	Do not eat, drink, or smoke during work.	Do NOT induce vomiting. Refer for medical attention.

SPILLAGE DISPOSAL	STORAGE	PACKAGING & LABELLING

Evacuate danger area! Collect leaking liquid in sealable containers. Absorb remaining liquid in sand or inert absorbent and remove to safe place.	Fireproof. Separated from strong oxidants. Cool. Keep in a well-ventilated room.	F symbol R: 11 S: 7-16 Note: C UN Hazard Class: 3 UN Packing Group: II

SEE IMPORTANT INFORMATION ON BACK

ICSC: 0554

Prepared in the context of cooperation between the International Programme on Chemical Safety & the Commission of the European Communities © IPCS CEC 1993 No modifications to the International version have been made except to add the OSHA PELs, NIOSH RELs and IDLH values.

International Chemical Safety Cards

ISOPROPYL ALCOHOL

ICSC: 0554

IMPORTANT DATA

PHYSICAL STATE; APPEARANCE:
CLEAR COLOURLESS LIQUID.

PHYSICAL DANGERS:
The vapour mixes well with air, explosive mixtures are easily formed.

CHEMICAL DANGERS:
Reacts with strong oxidants.

OCCUPATIONAL EXPOSURE LIMITS (OELs):
TLV: 400 ppm; 983 mg/m^3 (as TWA); 500 ppm; 1230 mg/m^3 (as STEL) (ACGIH 1991-1992).
OSHA PEL: TWA 400 ppm (980 mg/m^3)
NIOSH REL: TWA 400 ppm (980 mg/m^3) ST 500 ppm (1225 mg/m^3)
NIOSH IDLH: 2000 ppm LEL

ROUTES OF EXPOSURE:
The substance can be absorbed into the body by inhalation of its vapour, by inhalation of its aerosol and by ingestion.

INHALATION RISK:
A harmful contamination of the air can be reached rather quickly on evaporation of this substance at 20°C.

EFFECTS OF SHORT-TERM EXPOSURE:
The substance irritates the eyes, the skin and the respiratory tract. The substance may cause effects on the central nervous system , resulting in depression. Exposure far above the OEL may result in unconsciousness. The effects may be delayed. Medical observation is indicated.

EFFECTS OF LONG-TERM OR REPEATED EXPOSURE:
Repeated or prolonged contact with skin may cause dermatitis.

PHYSICAL PROPERTIES

Boiling point: 83°C
Melting point: -90°C
Relative density (water = 1): 0.79
Solubility in water: Miscible
Vapour pressure, kPa at 20°C: 4.4
Relative vapour density (air = 1): 2.1
Relative density of the vapour/air-mixture at 20°C (air = 1): 1.05
Flash point: 11.7°C
Auto-ignition temperature: 455°C
Explosive limits, vol% in air: 2-12
Octanol/water partition coefficient as log Pow: <0.28

ENVIRONMENTAL DATA

It is strongly advised not to let the chemical enter into the environment.



NOTES
Use of alcoholic beverages enhances the harmful effect. Transport Emergency Card: TEC (R)-544 NFPA Code: H 1; F 3; R 0;

ADDITIONAL INFORMATION	

ICSC: 0554 **ISOPROPYL ALCOHOL**

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IMPORTANT LEGAL NOTICE:	Neither NIOSH, the CEC or the IPCS nor any person acting on behalf of NIOSH, the CEC or the IPCS is responsible for the use which might be made of this information. This card contains the collective views of the IPCS Peer Review Committee and may not reflect in all cases all the detailed requirements included in national legislation on the subject. The user should verify compliance of the cards with the relevant legislation in the country of use. The only modifications made to produce the U.S. version is inclusion of the OSHA PELs, NIOSH RELs and IDLH values.

NTP CHEMICAL REPOSITORY (RADIAN CORPORATION, AUGUST 29, 1991)
ISOPROPANOL

-IDENTIFIERS
 ===========

*CATALOG ID NUMBER: 001880

*CAS NUMBER: 67-63-0

*BASE CHEMICAL NAME: ISOPROPANOL

*PRIMARY NAME: ISOPROPANOL

*CHEMICAL FORMULA: C3H8O

*STRUCTURAL FORMULA: CH3CH(OH)CH3

*WLN: QY1&1

*SYNONYMS:
  ISOPROPYL ALCOHOL
  DIMETHYLCARBINOL
  2-HYDROXYPROPANE
  PROPAN-2-OL
  2-PROPANOL
  SEC-PROPYL ALCOHOL
  ALCOJEL
  ALCOSOLVE
  AVANTIN
  AVANTINE
  CHROMAR
  COMBI-SCHUTZ
  HARTOSOL
  IMSOL A
  ISOHOL
  LUTOSOL
  PETROHOL
  PRO
  N-PROPAN-2-OL
  PROPOL
  2-PROPYL ALCOHOL
  SPECTRAR
  STERISOL HAND DISINFECTANT
  TAKINEOCOL
  UN 1219
  ALCOSOLVE 2

-PHYSICAL CHEMICAL DATA
 ======================

*PHYSICAL DESCRIPTION: LITERATURE: Clear colorless liquid
                       REPOSITORY: Clear colorless liquid

*MOLECULAR WEIGHT: 60.10

*SPECIFIC GRAVITY: 0.785 @ 20/4 C [055,371]

*DENSITY: Not available

*MP (DEG C): -88.5 C [029,031,051,371]

*BP (DEG C): 82.5 C [031,043,301,346]

*SOLUBILITIES:
WATER : >=100 mg/mL @ 22 C (RAD)

DMSO : >=100 mg/mL @ 22 C (RAD)

95% ETHANOL : >=100 mg/mL @ 22 C (RAD)

METHANOL : Not available

ACETONE : >=100 mg/mL @ 22 C (RAD)

TOLUENE : Not available

OTHER SOLVENTS:
Alcohol: Miscible [016,031,043,295]
Benzene: Soluble [016]
Chloroform: Miscible [031,043,295,430]
Ether: Miscible [031,043,062,295]
Salt solutions: Insoluble [031,043,051]
Glycerol: Miscible [295]

*VOLATILITY:
Vapor pressure: 33 mm Hg @ 20 C [051,058,062,421]; 40 mm Hg @ 23.8 C [301]
Vapor density : 2.07 [043,051,055]

*FLAMMABILITY(FLASH POINT):
This chemical has a flash point of 12 C (53 F) [031,036,043,451]. It is flammable. Fires involving this material can be controlled with a dry chemical, carbon dioxide or Halon extinguisher. The autoignition temperature is 399 C (750 F) [036,371,451].

*UEL: 12% [043,051,058,421] LEL: 2.0% [051,058,421,451]

*REACTIVITY:
This chemical reacts with air or oxygen to form dangerously unstable peroxides. Contact with 2-butanone increases the reaction rate for peroxide formation. A violent, explosive reaction occurs when it is heated with (aluminum isopropoxide + crotonaldehyde). It forms explosive mixtures with trinitromethane and hydrogen peroxide. This chemical reacts with barium perchlorate to form a highly explosive compound. It ignites on contact with dioxygenyl tetrafluoroborate, chromium trioxide and potassium-tert-butoxide. Vigorous reactions occur with (hydrogen + palladium), nitroform, oleum, $COCl_2$, aluminum triisopropoxide and oxidizers [043]. It also reacts explosively with phosgene in the presence of iron salts [451]. It is incompatible with acids, acid anhydrides, halogens and aluminum [269].

*STABILITY:
This chemical is sensitive to heat [043]. Solutions of this chemical in water, DMSO, 95% ethanol or acetone should be stable for 24 hours under normal lab conditions (RAD).

*OTHER PHYSICAL DATA:
Specific gravity: 0.78084 @ 25/4 C; 0.728 @ 83/4 C [031]
Specific gravity: 0.7874 @ 20/20 C [430]
Freezing point: -89.5 C [029,031,047,275]
Vapor pressure: 44 mm Hg @ 25 C [430]

Bitter taste [031,043,295]
Odor recognition threshold limit: 7.5 ppm [058]
Evaporation rate (n-butyl acetate = 1): 1.4 [058]
Boiling point: 67.8 C @ 400 mm Hg; 53.0 C @ 200 mm Hg [031]
Boiling point: 39.5 C @ 100 mm Hg; 30.5 C @ 60 mm Hg; 23.8 C @ 40 mm Hg [031]
Boiling point: 12.7 C @ 20 mm Hg; 2.4 C @ 10 mm Hg; -7.0 C @ 5 mm Hg [031]
Forms an azeotrope with water (boiling point: 80.37 C @ 760 mm Hg; density: 0.83361 @ 0/4 C) [031]
Specific heat: 0.65 cal/g [062]
Critical temperature: 235 C [051,371]
Critical pressure: 53 atmospheres [062]
Heat of combustion: 14346 Btu/lb [062]
Heat of vaporization: 288 Btu/lb [062]
Viscosity: 2.1 centipoise @ 25 C [062]
log P octanol: -0.16/0.28 (calculated) [055]
Slight odor [043,051]
Refractive index: 1.3852 @ 8 C; 1.3802 @ 15 C; 1.3749 @ 25 C [031]
Refractive index: 1.3776 @ 20 C [016,029,047]
Burning rate: 2.3 mm/min [371]

-TOXICITY
========

*NIOSH REGISTRY NUMBER: NT8050000

*TOXICITY:

typ. dose	mode	specie	amount	units	other
TDLo	orl	hmn	223	mg/kg	
LDLo	orl	man	5272	mg/kg	
LDLo	unr	man	2770	mg/kg	
LD50	orl	rat	5045	mg/kg	
LCLo	ihl	rat	16000	ppm/4H	
LD50	orl	mus	3600	mg/kg	
LD50	ipr	mus	4477	mg/kg	
LDLo	scu	mus	6000	mg/kg	
LD50	ivn	mus	1509	mg/kg	
LD50	orl	dog	4797	mg/kg	
LDLo	ivn	dog	5120	mg/kg	
LDLo	ivn	cat	1963	mg/kg	
LD50	orl	rbt	6410	mg/kg	
LD50	skn	rbt	12800	mg/kg	
LD50	ivn	rbt	1184	mg/kg	
LDLo	scu	mam	6	mg/kg	
TDLo	orl	man	14432	mg/kg	
LDLo	orl	hmn	3570	mg/kg	
LD50	ipr	rat	2735	mg/kg	
LD50	ivn	rat	1088	mg/kg	
LCLo	ihl	mus	12800	ppm/3H	
LD50	ipr	rbt	667	mg/kg	
LD50	ipr	gpg	2560	mg/kg	
LD50	ipr	ham	3444	mg/kg	
LDLo	par	frg	20	gm/kg	

*AQTX/TLM96: Not available

*SAX TOXICITY EVALUATION:
THR: Poison by ingestion and subcutaneous routes. Moderately toxic to humans by an unspecified route. Moderately toxic experimentally by intravenous and intraperitoneal routes. Mildly toxic by skin contact. Human systemic effects by ingestion or inhalation. Experi-

mental teratogenic and reproductive effects. Mutagenic data. An eye and skin irritant.

*CARCINOGENICITY:
Review: IARC Cancer Review: Human Inadequate Evidence
IARC Cancer Review: Animal Inadequate Evidence
IARC: Not classifiable as a human carcinogen (Group 3) [015,395,610]

*MUTATION DATA: See RTECS printout for data

*TERATOGENICITY: See RTECS printout for data

*STANDARDS, REGULATIONS & RECOMMENDATIONS:
OSHA: Federal Register (1/19/89) and 29 CFR 1910.1000 Subpart Z
Transitional Limit: PEL-TWA 400 ppm [015,327,545,610]
Final Limit: PEL-TWA 400 ppm; STEL 500 ppm [015,545,610]
ACGIH: TLV-TWA 400 ppm; STEL 500 ppm [015,415,421,610]
NIOSH Criteria Document: Recommended Exposure Limit to this compound-air: TWA 400 ppm/10H; Ceiling Limit 800 ppm/15M [015,610]
NFPA Hazard Rating: Health (H): 1
Flammability (F): 3
Reactivity (R): 0
H1: Materials only slightly hazardous to health (see NFPA for details).
F3: Materials which can be ignited under almost all normal temperature conditions (see NFPA for details).
R0: Materials which are normally stable even under fire exposure conditions and which are not reactive with water (see NFPA for details).

*OTHER TOXICITY DATA:
Skin and Eye Irritation Data:
eye-rbt 10 mg MOD
skn-rbt 500 mg MLD
eye-rbt 16 mg
eye-rbt 100 mg/24H MOD
Review: Toxicology Review-3
Standards and Regulations: DOT-Hazard: Flammable liquid; Label: Flammable liquid
Status: EPA Genetox Program 1988, Negative: Cell transform.-SA7/SHE; N crassa-aneuploidy
EPA TSCA Chemical Inventory, 1986
EPA TSCA Section 8(e) Status Report 8EHQ-1180-0371
EPA TSCA Section 8(e) Status Report 8EHQ-0985-0566
EPA Test Submission (TSCATS) Data Base, September 1989
NIOSH Analytical Methods: see Alcohols I, 1400
IDLH value: 20000 ppm [371]
Single lethal dose for adults is ~250 mLs although as little as 100 mLs can be fatal [043].

-OTHER DATA (Regulatory)
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*PROPER SHIPPING NAME (IATA): Isopropanol

*UN/ID NUMBER: UN1219

*HAZARD CLASS: 3 SUBSIDIARY RISK: None PACKING GROUP: II

*LABELS REQUIRED: Flammable liquid

*PACKAGING: PASSENGER: PKG. INSTR.: 305, Y305 MAXIMUM QUANTITY: 5 L, 1 L

CARGO : PKG. INSTR.: 307 MAXIMUM QUANTITY: 60 L

*SPECIAL PROVISIONS: None

*USES:
This compound is used as a solvent in perfumery and cosmetics, in the preservation of pathological specimens and dehydration of tissues, as a non-aqueous moistening agent for tablet granulation, in hair preparations, in lotions, in liniments, as a solvent for creosote, resins, gums, inks, oils, lotions, shellac and essential oils, as an antifreeze mixture and as an extraction solvent in food preparation. It is externally substituted for industrial methylated spirit and surgical spirit. It is also used in the extraction of alkaloids, in quick-drying oils, in quick-drying inks, in the denaturing of ethyl alcohol, in body rubs, in after-shave lotions, in the manufacture of acetone, glycerol and isopropyl acetate; as a pharmaceutic aid (solvent), as an antiseptic, as a rubefacient, as a deicing agent for liquid fuels, as a dehydrating agent, as a window cleaner, in permanent hair wave preparations, in dye solutions, as a disinfectant and in pliable ice packs.

*COMMENTS: Not available

-HANDLING PROCEDURES

*ACUTE/CHRONIC HAZARDS:
This compound is an irritant of the skin, eyes, mucous membranes and upper respiratory tract [269]. It is flammable and flashback along the vapor trail may occur [371]. When heated to decomposition it emits acrid smoke and toxic fumes of carbon monoxide, carbon dioxide and unidentified organic compounds [043,058,269].

*MINIMUM PROTECTIVE CLOTHING: Not available

*RECOMMENDED GLOVE MATERIALS:
GlovES+ Expert System Glove Types For The Neat (Undiluted) Chemical:
This chemical has not been tested for permeation by Radian Corporation; however, the GlovES+ expert system was used to extrapolate permeation test information from compounds in the same chemical class. The GlovES+ system uses permeation data from literature sources; therefore, extra safety margins should be used with the estimated protection time(s). If this chemical makes direct contact with your glove, or if a tear, puncture or hole develops, replace them at once.
The GlovES+ expert system is a tool that can help people better manage protection from chemicals, however this tool cannot replace sound judgment nor make technical decisions. Our GlovES+ expert system is designed to offer initial advice and assistance in glove selection while the final glove selection should be made by knowledgeable individuals based on the specific circumstances involved.

Glove Type	Model Number	Thickness	Estimated Protection Time
Neoprene	Ansell Neoprene 530	0.46 mm	360 min
Nitrile	Pioneer A-14	0.56 mm	480 min
PE/EVAL/PE	Safety4 4H	0.07 mm	240 min
PVC	Comasec Multitop	0.07 mm	480 min

*RECOMMENDED RESPIRATOR:
When working with this chemical, wear a NIOSH-approved full face chemical cartride respirator equipped with the appropriate organic vapor cartridges. If that is not available, a half face respirator similarly

equipped plus airtight goggles can be substituted. However, please note that half face respirators provide a substantially lower level of protection than do full face respirators.

*OTHER: Not available

*STORAGE PRECAUTIONS:
You should store this material in a refrigerator. STORE AWAY FROM SOURCES OF IGNITION.

*SPILLS AND LEAKAGE:
If you should spill this chemical, use absorbent paper to pick up all liquid spill material. Seal the absorbent paper, as well as any of your clothing which may be contaminated, in a vapor-tight plastic bag for eventual disposal. Wash any surfaces you may have contaminated with a soap and water solution. Do not reenter the contaminated area until the Safety Officer (or other responsible person) has verified that the area has been properly cleaned.

*DISPOSAL AND WASTE TREATMENT: Not available

-EMERGENCY PROCEDURES
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*SKIN CONTACT:
IMMEDIATELY flood affected skin with water while removing and isolating all contaminated clothing. Gently wash all affected skin areas thoroughly with soap and water.
If symptoms such as redness or irritation develop, IMMEDIATELY call a physician and be prepared to transport the victim to a hospital for treatment.

*INHALATION:
IMMEDIATELY leave the contaminated area; take deep breaths of fresh air. If symptoms (such as wheezing, coughing, shortness of breath, or burning in the mouth, throat, or chest) develop, call a physician and be prepared to transport the victim to a hospital.
Provide proper respiratory protection to rescuers entering an unknown atmosphere. Whenever possible, Self-Contained Breathing Apparatus (SCBA) should be used; if not available, use a level of protection greater than or equal to that advised under Respirator Recommendation.

*EYE CONTACT:
First check the victim for contact lenses and remove if present. Flush victim's eyes with water or normal saline solution for 20 to 30 minutes while simultaneously calling a hospital or poison control center.
Do not put any ointments, oils, or medication in the victim's eyes without specific instructions from a physician.
IMMEDIATELY transport the victim after flushing eyes to a hospital even if no symptoms (such as redness or irritation) develop.

*INGESTION:
DO NOT INDUCE VOMITING. Volatile chemicals have a high risk of being aspirated into the victim's lungs during vomiting which increases the medical problems.
If the victim is conscious and not convulsing, give 1 or 2 glasses of water to dilute the chemical and IMMEDIATELY call a hospital or poison control center. IMMEDIATELY transport the victim to a hospital.
If the victim is convulsing or unconscious, do not give anything by mouth, ensure that the victim's airway is open and lay the victim on his/her side with the head lower than the body. DO NOT INDUCE VOMITING. IMMEDIATELY transport

the victim to a hospital.

*SYMPTOMS:

Symptoms of exposure to this compound include irritation of the skin, eyes, nose, throat and respiratory tract, dizziness, nausea, central nervous system depression, dizziness, giddiness and headache [058]. It can cause flushing, decrease in pulse rate, lowered blood pressure, anesthesia, narcosis, mental depression, hallucinations, distorted perceptions, dyspnea, respiratory depression, vomiting, corneal burns, eye damage and coma [043]. It can also cause abdominal pain, hematemesis, areflexia, oliguria followed by diuresis, generalized tenderness, induration and edema of muscles. Prolonged skin contact may cause corrosion [301]. Drunkenness may also occur [371].

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=======

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New Jersey Department of Health and Senior Services

HAZARDOUS SUBSTANCE FACT SHEET

Common Name: **ISOPROPYL ALCOHOL**

CAS Number: 67-63-0
DOT Number: UN 1219

RTK Substance number: 1076
Date: February 1989 Revision: January 1997

HAZARD SUMMARY

* **Isopropyl Alcohol** can affect you when breathed in and by passing through your skin.
* There is an increased risk of cancer associated with the manufacture of **Isopropyl Alcohol**.
* Contact can irritate and burn the skin and eyes. Repeated skin exposure can cause itching, rash, drying and cracking.
* Breathing **Isopropyl Alcohol** can irritate the nose and throat.
* Overexposure can cause headache, drowsiness, unconsciousness and death.
* **Isopropyl Alcohol** is a FLAMMABLE LIQUID and a FIRE HAZARD.

IDENTIFICATION

Isopropyl Alcohol is a colorless liquid. It is used as a solvent and in making many commercial products. *Rubbing alcohol* is a solution of **Isopropyl Alcohol**.

REASON FOR CITATION

* **Isopropyl Alcohol** is on the Hazardous Substance List because it is regulated by OSHA and cited by ACGIH, DOT, NFPA and NIOSH.
* This chemical is on the Special Health Hazard Substance List because it is **FLAMMABLE**.
* Definitions are provided on page 5.

HOW TO DETERMINE IF YOU ARE BEING EXPOSED

The New Jersey Right to Know Act requires most employers to label chemicals in the workplace and requires public employers to provide their employees with information and training concerning chemical hazards and controls. The federal OSHA Hazard Communication Standard, 1910.1200, requires private employers to provide similar training and information to their employees.

* Exposure to hazardous substances should be routinely evaluated. This may include collecting air samples. Under OSHA 1910.20, you have a legal right to obtain copies of sampling results from your employer.
* If you think you are experiencing any work-related health problems, see a doctor trained to recognize occupational diseases. Take this Fact Sheet with you.

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* **ODOR THRESHOLD = 22 ppm**.
* The range of accepted odor threshold values is quite broad. Caution should be used in relying on odor alone as a warning of potentially hazardous exposures.

WORKPLACE EXPOSURE LIMITS

OSHA: The legal airborne permissible exposure limit (PEL) is **400 ppm** averaged over an 8-hour workshift.

NIOSH: The recommended airborne exposure limit is **400 ppm** averaged over a 10-hour workshift and **500 ppm** not to be exceeded during any 15 minute work period.

ACGIH: The recommended airborne exposure limit is **400 ppm** averaged over an 8-hour workshift and **500 ppm** as a STEL (short term exposure limit).

* The above exposure limits are for air levels only. When skin contact also occurs, you may be overexposed, even though air levels are less than the limits listed above.

WAYS OF REDUCING EXPOSURE

* Where possible, enclose operations and use local exhaust ventilation at the site of chemical release. If local exhaust ventilation or enclosure is not used, respirators should be worn.
* Wear protective work clothing.
* Wash thoroughly immediately after exposure to **Isopropyl Alcohol** and at the end of the workshift.
* Post hazard and warning information in the work area. In addition, as part of an ongoing education and training effort, communicate all information on the health and safety hazards of **Isopropyl Alcohol** to potentially exposed workers.

This Fact Sheet is a summary source of information of all potential and most severe health hazards that may result from exposure. Duration of exposure, concentration of the substance and other factors will affect your susceptibility to any of the potential effects described below.

HEALTH HAZARD INFORMATION

Acute Health Effects

The following acute (short-term) health effects may occur immediately or shortly after exposure to **Isopropyl Alcohol**:

* Contact can irritate and burn the skin and eyes.
* Breathing **Isopropyl Alcohol** can irritate the nose and throat.
* Overexposure can cause headache, drowsiness, a loss of coordination, unconsciousness and death.

Chronic Health Effects

The following chronic (long-term) health effects can occur at some time after exposure to **Isopropyl Alcohol** and can last for months or years:

Cancer Hazard

* There is an increased incidence of nasal sinus cancer in workers involved in the manufacture of **Isopropyl Alcohol** by the strong-acid process. However, **Isopropyl Alcohol** has been tested and has not been shown to cause cancer in animals.

Reproductive Hazard

* According to the information presently available to the New Jersey Department of Health and Senior Services, **Isopropyl Alcohol** has been tested and has not been shown to affect reproduction.

Other Long-Term Effects

* Repeated skin exposure can cause itching, redness, rash, drying and cracking.
* This chemical has not been adequately evaluated to determine whether brain or other nerve damage could occur with repeated exposure. However, many solvents and other petroleum-based chemicals have been shown to cause such damage. Effects may include reduced memory and concentration, personality changes (withdrawal, irritability), fatigue, sleep disturbances, reduced coordination, and/or effects on nerves supplying internal organs (autonomic nerves) and/or nerves to the arms and legs (weakness, "pins and needles").

MEDICAL

Medical Testing

If symptoms develop or overexposure is suspected, the following may be useful:

* There is no special test for this chemical. However, if illness occurs or overexposure is suspected, medical attention is recommended.
* Interview for brain effects, including recent memory, mood (irritability, withdrawal), concentration, headaches, malaise and altered sleep patterns. Consider cerebellar, autonomic and peripheral nervous system evaluation. Positive and borderline individuals should be referred for neuropsychological testing.

Any evaluation should include a careful history of past and present symptoms with an exam. Medical tests that look for damage already done are not a substitute for controlling exposure.

Request copies of your medical testing. You have a legal right to this information under OSHA 1910.20.

WORKPLACE CONTROLS AND PRACTICES

Unless a less toxic chemical can be substituted for a hazardous substance, **ENGINEERING CONTROLS** are the most effective way of reducing exposure. The best protection is to enclose operations and/or provide local exhaust ventilation at the site of chemical release. Isolating operations can also reduce exposure. Using respirators or protective equipment is less effective than the controls mentioned above, but is sometimes necessary.

In evaluating the controls present in your workplace, consider: (1) how hazardous the substance is, (2) how much of the substance is released into the workplace and (3) whether harmful skin or eye contact could occur. Special controls should be in place for highly toxic chemicals or when significant skin, eye, or breathing exposures are possible.

In addition, the following controls are recommended:

* Where possible, automatically pump liquid **Isopropyl Alcohol** from drums or other storage containers to process containers.
* Specific engineering controls are recommended for this chemical by NIOSH. Refer to the NIOSH criteria document: *Isopropyl Alcohol #76-142*.
* Before entering a confined space where **Isopropyl Alcohol** may be present, check to make sure that an explosive concentration does not exist.

Good **WORK PRACTICES** can help to reduce hazardous exposures. The following work practices are recommended:

* Workers whose clothing has been contaminated by **Isopropyl Alcohol** should change into clean clothing promptly.
* Contaminated work clothes should be laundered by individuals who have been informed of the hazards of exposure to **Isopropyl Alcohol**.
* On skin contact with **Isopropyl Alcohol**, immediately wash or shower to remove the chemical. At the end of the workshift, wash any areas of the body that may have contacted **Isopropyl Alcohol**, whether or not known skin contact has occurred.
* Do not eat, smoke, or drink where **Isopropyl Alcohol** is handled, processed, or stored, since the chemical can be swallowed. Wash hands carefully before eating or smoking.

PERSONAL PROTECTIVE EQUIPMENT

WORKPLACE CONTROLS ARE BETTER THAN PERSONAL PROTECTIVE EQUIPMENT. However, for some jobs (such as outside work, confined space entry, jobs done only once in a while, or jobs done while workplace controls are being installed), personal protective equipment may be appropriate.

The following recommendations are only guidelines and may not apply to every situation.

Clothing

* Avoid skin contact with **Isopropyl Alcohol**. Wear solvent-resistant gloves and clothing. Safety equipment suppliers/manufacturers can provide recommendations on the most protective glove/clothing material for your operation.
* All protective clothing (suits, gloves, footwear, headgear) should be clean, available each day, and put on before work.
* ACGIH recommends *Natural Rubber, Neoprene, Nitrile* or *Polyvinyl Chloride* as protective materials.

Eye Protection

* Wear splash-proof chemical goggles and face shield when working with liquid, unless full facepiece respiratory protection is worn.

Respiratory Protection

IMPROPER USE OF RESPIRATORS IS DANGEROUS. Such equipment should only be used if the employer has a written program that takes into account workplace conditions, requirements for worker training, respirator fit testing and medical exams, as described in OSHA 1910.134.

* Where the potential exists for exposures over **400 ppm**, use a MSHA/ NIOSH approved full facepiece respirator with an organic vapor cartridge/canister. Even greater protection is provided by a powered-air purifying respirator.
* If while wearing a filter, cartridge or canister respirator, you can smell, taste, or otherwise detect **Isopropyl Alcohol**, or in the case of a full facepiece respirator you experience eye irritation, leave the area immediately. Check to make sure the respirator-to-face seal is still good. If it is, replace the filter, cartridge, or canister. If the seal is no longer good, you may need a new respirator.
* Be sure to consider all potential exposures in your workplace. You may need a combination of filters, prefilters, cartridges, or canisters to protect against different forms of a chemical (such as vapor and mist) or against a mixture of chemicals.
* Where the potential for high exposures exists, use a MSHA/NIOSH approved supplied-air respirator with a full facepiece operated in a pressure-demand or other positive-pressure mode. For increased protection use in combination with an auxiliary self-contained breathing apparatus operated in a pressure-demand or other positive-pressure mode.
* Exposure to **2,000 ppm** is immediately dangerous to life and health. If the possibility of exposure above **2,000 ppm** exists, use a MSHA/NIOSH approved self-contained breathing apparatus with a full facepiece operated in continuous flow or other positive pressure mode.

HANDLING AND STORAGE

* Prior to working with **Isopropyl Alcohol** you should be trained on its proper handling and storage.
* **Isopropyl Alcohol** must be stored to avoid contact with STRONG OXIDIZERS (such as CHLORINE, BROMINE and FLUORINE) since violent reactions occur.

* Store in tightly closed containers in a cool, well-ventilated area away from HEAT.
* Sources of ignition, such as smoking and open flames, are prohibited where **Isopropyl Alcohol** is used, handled, or stored in a manner that could create a potential fire or explosion hazard.
* Metal containers involving the transfer of **Isopropyl Alcohol** should be grounded and bonded.
* Use only non-sparking tools and equipment, especially when opening and closing containers of **Isopropyl Alcohol**.

QUESTIONS AND ANSWERS

Q: If I have acute health effects, will I later get chronic health effects?
A: Not always. Most chronic (long-term) effects result from repeated exposures to a chemical.

Q: Can I get long-term effects without ever having short-term effects?
A: Yes, because long-term effects can occur from repeated exposures to a chemical at levels not high enough to make you immediately sick.

Q: What are my chances of getting sick when I have been exposed to chemicals?
A: The likelihood of becoming sick from chemicals is increased as the amount of exposure increases. This is determined by the length of time and the amount of material to which someone is exposed.

Q: When are higher exposures more likely?
A: Conditions which increase risk of exposure include physical and mechanical processes (heating, pouring, spraying, spills and evaporation from large surface areas such as open containers), and "confined space" exposures (working inside vats, reactors, boilers, small rooms, etc.).

Q: Is the risk of getting sick higher for workers than for community residents?
A: Yes. Exposures in the community, except possibly in cases of fires or spills, are usually much lower than those found in the workplace. However, people in the community may be exposed to contaminated water as well as to chemicals in the air over long periods. Because of this, and because of exposure of children or people who are already ill, community exposures may cause health problems.

The following information is available from:

New Jersey Department of Health and
Senior Services
Occupational Disease and Injury Services
Trenton, NJ 08625-0360
(609) 984-1863

Industrial Hygiene Information

Industrial hygienists are available to answer your questions regarding the control of chemical exposures using exhaust ventilation, special work practices, good housekeeping, good hygiene practices, and personal protective equipment including respirators. In addition, they can help to interpret the results of industrial hygiene survey data.

Medical Evaluation

If you think you are becoming sick because of exposure to chemicals at your workplace, you may call a Department of Health and Senior Services physician who can help you find the services you need.

Public Presentations

Presentations and educational programs on occupational health or the Right to Know Act can be organized for labor unions, trade associations and other groups.

Right to Know Information Resources

The Right to Know Infoline (609) 984-2202 can answer questions about the identity and potential health effects of chemicals, list of educational materials in occupational health, references used to prepare the Fact Sheets, preparation of the Right to Know survey, education and training programs, labeling requirements, and general information regarding the Right to Know Act. Violations of the law should be reported to (609) 984-2202.

DEFINITIONS

ACGIH is the American Conference of Governmental Industrial Hygienists. It recommends upper limits (called TLVs) for exposure to workplace chemicals.

A **carcinogen** is a substance that causes cancer.

The **CAS number** is assigned by the Chemical Abstracts Service to identify a specific chemical.

A **combustible** substance is a solid, liquid or gas that will burn.

A **corrosive** substance is a gas, liquid or solid that causes irreversible damage to human tissue or containers.

DEP is the New Jersey Department of Environmental Protection.

DOT is the Department of Transportation, the federal agency that regulates the transportation of chemicals.

EPA is the Environmental Protection Agency, the federal agency responsible for regulating environmental hazards.

A **fetus** is an unborn human or animal.

A **flammable** substance is a solid, liquid, vapor or gas that will ignite easily and burn rapidly.

The **flash point** is the temperature at which a liquid or solid gives off vapor that can form a flammable mixture with air.

HHAG is the Human Health Assessment Group of the federal EPA.

IARC is the International Agency for Research on Cancer, a scientific group that classifies chemicals according to their cancer-causing potential.

A **miscible** substance is a liquid or gas that will evenly dissolve in another.

mg/m^3 means milligrams of a chemical in a cubic meter of air. It is a measure of concentration (weight/volume).

MSHA is the Mine Safety and Health Administration, the federal agency that regulates mining. It also evaluates and approves respirators.

A **mutagen** is a substance that causes mutations. A **mutation** is a change in the genetic material in a body cell. Mutations can lead to birth defects, miscarriages, or cancer.

NAERG is the North American Emergency Response Guidebook. It was jointly developed by Transport Canada, the United States Department of Transportation and the Secretariat of Communications and Transportation of Mexico. It is a guide for first responders to quickly identify the specific or generic hazards of material involved in a transportation incident, and to protect themselves and the general public during the initial response phase of the incident.

NCI is the National Cancer Institute, a federal agency that determines the cancer-causing potential of chemicals.

NFPA is the National Fire Protection Association. It classifies substances according to their fire and explosion hazard.

NIOSH is the National Institute for Occupational Safety and Health. It tests equipment, evaluates and approves respirators, conducts studies of workplace hazards, and proposes standards to OSHA.

NTP is the National Toxicology Program which tests chemicals and reviews evidence for cancer.

OSHA is the Occupational Safety and Health Administration, which adopts and enforces health and safety standards.

PEOSHA is the Public Employees Occupational Safety and Health Act, a state law which sets PELs for New Jersey public employees.

ppm means parts of a substance per million parts of air. It is a measure of concentration by volume in air.

A **reactive** substance is a solid, liquid or gas that releases energy under certain conditions.

A **teratogen** is a substance that causes birth defects by damaging the fetus.

TLV is the Threshold Limit Value, the workplace exposure limit recommended by ACGIH.

The **vapor pressure** is a measure of how readily a liquid or a solid mixes with air at its surface. A higher vapor pressure indicates a higher concentration of the substance in air and therefore increases the likelihood of breathing it in.

>>>>>>>>>>>>>>>>> E M E R G E N C Y I N F O R M A T I O N <<<<<<<<<<<<<<<<<

Common Name: **ISOPROPYL ALCOHOL**
DOT Number: **UN 1219**
NAERG Code: **129**
CAS Number: **67-63-0**

Hazard rating	NJ DOH	NFPA
FLAMMABILITY	-	3
REACTIVITY	-	0
POISONOUS GASES ARE PRODUCED IN FIRE CONTAINERS MAY EXPLODE IN FIRE		

Hazard Rating Key: 0=minimal; 1=slight; 2=moderate; 3=serious; 4=severe

FIRE HAZARDS

* **Isopropyl Alcohol** is a FLAMMABLE LIQUID.
* Vapors may travel to a source of ignition and flash back.
* CONTAINERS MAY EXPLODE IN FIRE.
* Use dry chemical, CO_2, water spray, or alcohol foam extinguishers.
* POISONOUS GASES ARE PRODUCED IN FIRE.
* If employees are expected to fight fires, they must be trained and equipped as stated in OSHA 1910.156.

SPILLS AND EMERGENCIES

If **Isopropyl Alcohol** is spilled or leaked, take the following steps:

* Restrict persons not wearing protective equipment from area of spill or leak until clean-up is complete.
* Remove all ignition sources.
* Ventilate area of spill or leak.
* Absorb liquids in vermiculite, dry sand, earth, or a similar material and deposit in sealed containers.
* Keep **Isopropyl Alcohol** out of a confined space, such as a sewer, because of the possibility of an explosion, unless the sewer is designed to prevent the build-up of explosive concentrations.
* It may be necessary to contain and dispose of **Isopropyl Alcohol** as a HAZARDOUS WASTE. Contact your Department of Environmental Protection (DEP) or your regional office of the federal Environmental Protection Agency (EPA) for specific recommendations.
* If employees are required to clean-up spills, they must be properly trained and equipped. OSHA 1910.120(q) may be applicable.

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FOR LARGE SPILLS AND FIRES immediately call your fire department. You can request emergency information from the following:

CHEMTREC: (800) 424-9300
NJDEP HOTLINE: (609) 292-7172

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HANDLING AND STORAGE (See page 3)

FIRST AID

In NJ, POISON INFORMATION 1-800-962-1253

Eye Contact

* Immediately flush with large amounts of water for at least 15 minutes, occasionally lifting upper and lower lids.

Skin Contact

* Quickly remove contaminated clothing. Immediately wash contaminated skin with large amounts of water.

Breathing

* Remove the person from exposure.
* Begin rescue breathing if breathing has stopped and CPR if heart action has stopped.
* Transfer promptly to a medical facility.

PHYSICAL DATA

Vapor Pressure: 33 mm Hg at 68^{o}F (20^{o}C)
Flash Point: 53^{o}F (11.6^{o}C)
Water Solubility: Miscible

OTHER COMMONLY USED NAMES

Chemical Name:

2-Propanol

Other Names:

Dimethylcarbinol; Isopropanol; sec-Propyl Alcohol

Not intended to be copied and sold for commercial purposes.

NEW JERSEY DEPARTMENT OF HEALTH AND
SENIOR SERVICES
Right to Know Program
CN 368, Trenton, NJ 08625-0368
(609) 984-2202

Web Sites

that offer searchable chemical databases, recommended by Scorecard

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If you want more detailed information about a chemical than Scorecard provides, there are several on-line and library resources Scorecard recommends for further research.

ON-LINE CHEMICAL DATABASES

CambridgeSoft Chemfinder
http://chemfinder.camsoft.com/

Search

Chemfinder gives basic physico-chemical data and molecular structures for chemicals, and provides links to international data sources addressing specific chemicals.

Hazardous Substances Data Bank
http://toxnet.nlm.nih.gov/

Search

HSDB focuses on the toxicology of potentially hazardous chemicals, and includes peer-reviewed information on human exposure, industrial hygiene, emergency handling procedures, environmental fate, and regulatory requirements.

University of Akron Hazardous Chemicals Database
http://ull.chemistry.uakron.edu/erd/

Search

The Hazardous Chemicals Database provides physical data on chemicals and links to Department of Transportation safety guides that are valuable for emergency response.

BIBLIOGRAPHIC RESOURCES ON CHEMICAL TOXICITY

Scorecard provides qualitative summaries of the health hazards posed by a chemical (e.g., it is a suspected neurotoxicant), but not direct access to supporting toxicological data. These scientific studies are abstracted in several toxicity databases, which are available in libraries, from commercial vendors, and sometimes on-line. The major toxicity databases include:

The Registry of Toxic Effects of Chemicals Substances (RTECS)
RTECS is a database of toxicological information compiled by the National Institute for Occupational Safety and Health. It contains summary information about the types of health effects chemicals can cause and the concentrations at which toxicity is known to occur. It is available from several commercial vendors at http://www.cdc.gov/niosh/rtecs.html, and can often be found at major public or university libraries.

TOXLINE
Free access to the National Library of Medicine's toxicology-specific database of abstracts, reference journal articles, and reports is available at http://www.medscape.com/misc/FormToxlineInfLive.html

MEDLINE

Free access to the National Library of Medicine's MEDLINE database of more than 9 million references to articles published in 3800 biomedical journals is available at http://www.nlm.nih.gov/databases/freemedl.html. Two Web-based products, PubMed and Internet Grateful Med, provide this access. Medline can also be accessed at http://www.medscape.com/misc/FormMedlineInfLive.html

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ISOPROPYL ALCOHOL (STRONG-ACID PROCESS) (EDF-377)

summary from the About the Chemicals section of Scorecard

- **Human Health Hazards** **Reference(s)**
  Recognized: --
  Suspected: Carcinogen IARC
  Neurotoxicant EPA-SARA
- **Hazard Rankings**
  Data lacking; not ranked by any system in Scorecard.
- **Chemical Use Profile**
  No data on industrial or consumer use in Scorecard.
- **Profile of Environmental Release and Waste Generation**
  No data on environmental releases in Scorecard.
- **Regulatory Coverage**
  Not on chemical lists in Scorecard.
- **Basic Testing to Identify Chemical Hazards**
  Information on whether basic tests to identify chemical hazards have been conducted on this chemical is not available.
- **Information Needed for Safety Assessment**
  Lacks at least some of the national data required for safety assessment.
  No data on risk assessment values in Scorecard.
- **Links**
  Other web sites specific to this chemical:

  - CalEPA Air Resources Board Toxic Air Contaminant Summary
  - IPCS International Chemical Safety Card
  - National Toxicology Program Health and Safety Information Sheet
  - New Jersey Fact Sheet

  If none of these sources meet your needs, you can try searching some other chemical database Web sites.

- **Notes**

TRI release and waste generation data are not available even though this compound is covered by TRI reporting requirements because the strong acid manufacturing process is no longer in use anywhere in the U.S.

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ETHYLBENZENE (100-41-4)

summary from the About the Chemicals section of Scorecard

- **Human Health Hazards**

		Reference(s)
Recognized:	--	
Suspected:	Cardiovascular or Blood Toxicant	RTECS
	Developmental Toxicant	EPA-HEN EPA-SARA OEHHA-2000
	Endocrine Toxicant	OEHHA-2000
	Gastrointestinal or Liver Toxicant	OEHHA-2000 RTECS
	Kidney Toxicant	OEHHA-2000 RTECS
	Neurotoxicant	DAN EPA-HEN RTECS
	Reproductive Toxicant	EPA-SARA
	Respiratory Toxicant	EPA-HEN RTECS
	Skin or Sense Organ Toxicant	EPA-HEN RTECS

- **Hazard Rankings**

  More hazardous than most chemicals in 3 out of 10 ranking systems.

- **Chemical Use Profile**

  This is a high volume chemical with production exceeding 1 million pounds annually in the U.S.
  Used in at least 6 industries.
  Used in consumer products, building materials or furnishings that contribute to indoor air pollution.

- **Profile of Environmental Release and Waste Generation**

  For a list of the geographic areas, facilities, or industrial sectors which report the largest releases or transfers of this chemical to the Toxics Release Inventory, select what you want:

  - Rank States
  - Rank Counties
  - Rank Zip Codes
  - Rank Facilities
  - Rank Industrial Sectors

- **Regulatory Coverage**

  On at least 6 federal regulatory lists.

- **Basic Testing to Identify Chemical Hazards**

  Eight basic tests to identify chemical hazards have been conducted and are publicly

available for this chemical.

- **Information Needed for Safety Assessment**

  Possesses all the national data required for safety assessment.
  Scorecard has risk assessment data for this chemical.

- **Links**

  Additional information about this chemical may be available elsewhere in Scorecard.

  Other web sites specific to this chemical:

  - Agency for Toxic Substances and Disease Registry Public Health Statement
  - CalEPA Air Resources Board Toxic Air Contaminant Summary
  - EPA Health Effects Notebook for Hazardous Air Pollutants
  - EPA Integrated Risk Information System Report
  - EPA Office of Ground Water and Drinking Water Contaminant Fact Sheet
  - Environmental Writer Chemical Backgrounder
  - IPCS International Chemical Safety Card
  - International Toxicity Estimates for Risk (ITER) from the Toxicology Excellence for Risk Assessment
  - National Toxicology Program Health and Safety Information Sheet
  - New Jersey Fact Sheet

  If none of these sources meet your needs, you can try searching some other chemical database Web sites.

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Endocrine Toxicity Definition

from the Health Effects section of Scorecard

Endocrine toxicity is defined as adverse effects on the structure and /or functioning of the endocrine system that result from exposure to chemical substances. The endocrine system is composed of many organs and glands that secrete hormones directly into the bloodstream, including the pituitary, hypothalamus, thyroid, adrenals, pancreas, thymus, ovaries, and testes. Once synthesized, hormones are conveyed to a target tissue, where they function as chemical messengers that transmit information between cells. Hormone levels and interactions control normal physiological processes, maintaining the body's homeostasis. Because the endocrine system is complex, a toxicant may interfere at any of a number of points along a hormone's pathway of production, regulation, and action. Some chemicals may injure the glands that synthesize and secrete hormones, while others disrupt hormonal actions at the target organ. Compounds that are toxic to the endocrine system may cause diseases such as hypothyroidism, diabetes mellitus, hypoglycemia, reproductive disorders, and cancer.

A wide variety of toxic substances can disrupt the function of the endocrine system. For example, chemicals that resemble the hormone estrogen can bind to estrogen receptors located throughout the body and either mimic the natural hormone or inhibit its actions. Exposure to endocrine-disrupting chemicals such as polychlorinated biphenyls (PCBs) and DDT have caused a host of toxic effects in wildlife, including impaired reproduction and development. Other endocrine toxicants, such as persistent organochlorine pesticides and dioxins, are being studied for their possible role in promoting hormone-induced cancers (such as breast cancer) and in lowering sperm counts and male fertility.

Specific organs and glands in the endocrine system are known to be damaged by chemical toxicants. Several chemicals and drugs can be toxic to the cells of the pancreas that produce insulin. Exposure to the rodenticide Vacor (N-3-pyridylmethyl-N'-p-nitrophenyl urea) can interfere with the secretion and function of pancreatic hormones, resulting in diabetes mellitus and hyperglycemia. Polyhydroxyphenols and the therapeutic drug lithium can disrupt thyroid gland function and cause hypothyroidism and goiter. Endocrine and reproductive dysfunction have been reported in men exposed to inorganic lead. Chronic exposure to lead can cause direct testicular toxicity, followed by hypothalamic or pituitary gland disturbances.

For further general information on chemicals and endocrine toxicity, see the following references:

Barsano, C. P., and J. Thomas. Endocrine Disorders of Occupational and Environmental Origin. Occupational Medicine. 7:3 479-502. 1992.

Birnbaum, L. S. Developmental Effects of Dioxins and Related Endocrine Disrupting Chemicals. Toxicology Letters. 82/83: 743-750. 1995.

Colborn, T., and C. Clement, eds. Chemically-Induced Alterations in Sexual and Functional Development: The Wildlife/Human Connection. Advances in Modern Environmental Toxicology, vol. 21. Princeton, N.J.: Princeton Scientific Publishing, 1992.

US Environmental Protection Agency Risk Assessment Forum. Special Report on Environmental Endocrine Disruption: An Effects Assessment and Analysis. 1997. Available at http://www.epa.gov/ORD/WebPubs/endocrine/

More

- references used to compile the list of endocrine toxicants
- list of endocrine toxicants

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Endocrine Toxicity References

from the Health Effects section of Scorecard

There is no generally accepted source for an authoritative list of chemicals that are recognized to cause endocrine toxicity.

EDF's list of suspect endocrine toxicants is compiled from the following sources:

BRUC: Brucker-Davis, F. Effects of Environmental Synthetic Chemicals on Thyroid Function. Thyroid. 8(9): 827-856. 1998.

EDF: See EDF's Custom Hazard Identification documentation.

EPA-HEN: US Environmental Protection Agency. Health Effects Notebook for Hazardous Air Pollutants. Review Draft. December 1994. http://www. epa.gov/ttn/uatw/hapindex.html

EPA-SDWA: US Environmental Protection Agency. Announcement of the Draft Drinking Water Contaminant Candidate List; Notice. 62 Federal Register 52193-52219 (October 6, 1997). (Table 6).

EPA-TRI: US Environmental Protection Agency. Addition of Certain Chemicals; Toxic Chemical Release Reporting; Community Right to Know. Proposed and Final Rules. 59 Federal Register 1788 (Jan 12, 1994); 59 Federal Register 61432 (November 30, 1994).

GUIL: Guillette, L. J., and E. Guillette. Environmental Contaminants and Reproductive Abnormalities in Wildlife: Implications for Public Health? Toxicology and Industrial Health. 12(3): 537-550. 1996.

HEAST: EPA, Office of Research and Development. Health Effects Assessment Summary Tables. Electronic Handbook of Risk Assessment Values 9(6):6/30/00. Electronic Handbook Publishers, Redmond, WA. http://www.wolfenet.com/~sdwyer/ehrav.htm

IL-EPA: Illinois EPA. Endocrine Disruptors Strategy. 1997. (Table 1: Preliminary List of Chemicals Associated with Endocrine System Effects in Animals and Humans or In Vitro). http://www.nihs.go.jp/hse/environ/illiepatable.htm

KEIT: Keith, L.H. (ed.). Environmental Endocrine Disruptors. John Wiley & Sons, NY. 1997.

NJ-FS: New Jersey Department of Health Services. Right to Know Program, NJDOH, Trenton, NJ. http://www.state.nj.us/health/eoh/rtkweb/

OEHHA-2000: Office of Environmental Health Hazard Assessment, California Environmental Protection Agency. Air Toxics Hot Spots Program Risk Assessment Guidelines, Part III. February, 2000 (http://www.oehha.ca.gov/air/chronic_rels/22RELS2k.html) and May, 2000 (http://www.oehha.ca.gov/air/chronic_rels/42kChREL.html)

OEHHA-99: Office of Environmental Health Hazard Assessment, California Environmental Protection Agency. Air Toxics Hot Spots Program Risk Assessment Guidelines, Part III, Draft Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels. June 1999 (http://www.oehha.ca.gov/air/chronic_rels/RAGSII.html) and October, 1999

(http://www.oehha.ca.gov/air/chronic_rels/RAGSp3draft.html).

OEHHA-97: Office of Environmental Health Hazard Assessment, California Environmental Protection Agency. Draft Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels. October 1997. http://www.oehha.org/air/chronic_rels/GETRELS.html

RTECS: National Institute for Occupational Safety and Health's Registry of Toxic Effects of Chemical Substances. See EDF's Suspect Hazard Identification documentation.

WWF: World Wildlife Fund. Our Stolen Future Chemical List. http://www.osf-facts.org/basics/chemlist.html. The WWF list is derived from references detailed at http://www.osf-facts.org/othersrc/prnthum.html and was originally published in: Colborn, T., F.S. vom Saal, and A.M. Soto. Developmental Effects of Endocrine-Disrupting Chemicals In Wildlife and Humans. Environmental Health Perspectives 101(5): 378-384. 1993.

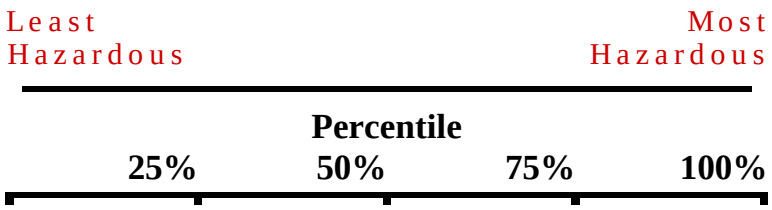
More

- definition of endocrine toxicity
- list of endocrine toxicants

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Hazard Rankings

for ETHYLBENZENE (100-41-4) from Scorecard



Human Health Rankings

Toxicity only

- Ingestion Toxicity Weight (RSEI)
- Inhalation Toxicity Weight (RSEI)
- Human Health Effects Score (UTN)

Toxicity and exposure potential

- Noncancer Risk Score - Air Releases (EDF)
- Noncancer Risk Score - Water Releases (EDF)
- Worker Exposure Hazard Score (IRCH)

Ecological Health Rankings

Toxicity only

- Ecological Effects Score (UTN)

Toxicity and persistence

- Environmental Hazard Value Score (IRCH)

Integrated Environmental Rankings

Combined human and ecological scores

- Total Hazard Value Score (IRCH)
- Total Hazard Value Score (UTN)

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Industrial Uses

for ETHYLBENZENE (100-41-4) from Scorecard

This is a high volume chemical with production exceeding 1 million pounds annually in the U.S.

Which Industries Use This Chemical?	**How is the Chemical Used in This Industry?**
Electroplating	Electroplating - Vapor Degreasing Solvents
Machinery Mfg and Repair	Solvents - Machinery Manufacture and Repair
Paint Manufacture	Hydrocarbon Solvents
Paper Coating	Solvents
Rubber Manufacture	Solvents - Rubber Manufacture
Wood Stains and Varnishes	Varnish Solvents

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Consumer Products

that contain ETHYLBENZENE (100-41-4) from Scorecard

What kinds of consumer products may contain this chemical?

- Aerosol paint concentrates
- Agricultural chemicals
- Auto, other transportation, and machinery refinish paints incl primers
- Automobile body polish and cleaners
- Bathroom tub and tile cleaners
- Building and construction plastic foam insulation, incl pipe and block
- Floor polish
- Furniture polish and cleaners
- Ground/traffic marking coatings
- Herbicides for agric., garden and health service use
- Insecticides for agric., garden and health service use
- Insecticides for crawling insects
- Insecticides for flying insects
- Laundry starch preparations
- Loose mineral wool fiber (blowing and pouring)
- Miscellaneous paint-related products
- Nonstructural caulking compounds and sealants
- Other automotive chemicals
- Other rubber floor and wall coverings incl cove base, wainscotting, etc.
- Other specialty cleaning and sanitation products
- Oven cleaners
- Paint and varnish removers
- Paint thinners
- Rug and upholstery cleaners
- Scatter rugs, bathmats, and sets (rugs 6 x 9 ft and smaller)
- Sheet vinyl flooring
- Solvent thinned exterior stains incl shingle and shake
- Solvent thinned exterior undercoaters and primers
- Solvent thinned interior clear finishes
- Solvent thinned interior stains
- Solvent thinned interior undercoaters and primers
- Waterproofing compounds

- Wood office furniture

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States with Reported Total Environmental Releases

of ETHYLBENZENE (100-41-4) from the About The Chemicals section of Scorecard

---

Ranked by (select your ranking criteria)

Total environmental releases Go (explain)

1. TEXAS: 1,696,672 Pounds
2. MICHIGAN: 1,019,004 Pounds
3. MISSOURI: 716,846 Pounds
4. OHIO: 560,576 Pounds
5. INDIANA: 482,341 Pounds
6. ILLINOIS: 375,028 Pounds
7. MISSISSIPPI: 340,068 Pounds
8. LOUISIANA: 328,492 Pounds
9. TENNESSEE: 300,240 Pounds
10. GEORGIA: 297,523 Pounds
11. KENTUCKY: 266,477 Pounds
12. ALABAMA: 256,585 Pounds
13. KANSAS: 223,187 Pounds
14. OKLAHOMA: 221,411 Pounds
15. VIRGINIA: 195,690 Pounds
16. PENNSYLVANIA: 179,737 Pounds
17. IOWA: 168,167 Pounds
18. MINNESOTA: 167,098 Pounds
19. WISCONSIN: 143,019 Pounds
20. ARKANSAS: 115,483 Pounds
21. NEW JERSEY: 111,456 Pounds
22. NEW HAMPSHIRE: 109,732 Pounds
23. MARYLAND: 103,387 Pounds
24. WEST VIRGINIA: 101,756 Pounds
25. NEW YORK: 81,627 Pounds
26. CALIFORNIA: 80,247 Pounds
27. SOUTH CAROLINA: 78,857 Pounds
28. FLORIDA: 77,145 Pounds

29. OREGON: 54,730 Pounds
30. NEW MEXICO: 54,708 Pounds
31. NEBRASKA: 54,180 Pounds
32. WASHINGTON: 50,564 Pounds
33. NORTH CAROLINA: 40,298 Pounds
34. SOUTH DAKOTA: 38,836 Pounds
35. PUERTO RICO: 32,143 Pounds
36. DELAWARE: 31,705 Pounds
37. VIRGIN ISLANDS: 24,824 Pounds
38. NORTH DAKOTA: 24,226 Pounds
39. WYOMING: 23,189 Pounds
40. MONTANA: 16,834 Pounds
41. CONNECTICUT: 15,483 Pounds
42. ALASKA: 14,077 Pounds
43. MASSACHUSETTS: 8,819 Pounds
44. UTAH: 5,741 Pounds
45. COLORADO: 5,054 Pounds
46. HAWAII: 4,570 Pounds
47. ARIZONA: 3,016 Pounds
48. RHODE ISLAND: 2,648 Pounds
49. MAINE: 2,130 Pounds
50. NEVADA: 1,248 Pounds
51. VERMONT: 750 Pounds
52. IDAHO: 576 Pounds
53. GUAM: 276 Pounds
54. AMERICAN SAMOA: 102 Pounds
55. NORTHERN MARIANA ISLANDS: 5 Pounds

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Counties with Reported Total Environmental Releases

of ETHYLBENZENE (100-41-4) from the About The Chemicals section of Scorecard

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Ranked by (select your ranking criteria)

Total environmental releases

in

Entire United States Go (explain)

1. HARRIS, TX: 1,074,220 pounds
2. CLAY, MO: 307,182 pounds
3. WAYNE, MI: 246,130 pounds
4. ST. LOUIS, MO: 184,508 pounds
5. KENT, MI: 175,322 pounds
6. COOK, IL: 166,303 pounds
7. JEFFERSON, KY: 144,866 pounds
8. GENESEE, MI: 140,351 pounds
9. LOWNDES, MS: 138,396 pounds
10. MACOMB, MI: 121,294 pounds
11. ROCKINGHAM, NH: 109,652 pounds
12. NORFOLK (CITY), VA: 108,733 pounds
13. JEFFERSON, TX: 102,220 pounds
14. LUCAS, OH: 102,034 pounds
15. OKLAHOMA, OK: 97,761 pounds
16. BRAZORIA, TX: 95,610 pounds
17. RAMSEY, MN: 94,653 pounds
18. DEKALB, GA: 91,058 pounds
19. CADDO, LA: 84,073 pounds
20. FULTON, GA: 81,432 pounds
21. BALTIMORE (CITY), MD: 79,326 pounds
22. WYANDOTTE, KS: 78,827 pounds
23. OAKLAND, MI: 77,550 pounds
24. ST. CHARLES, MO: 76,900 pounds
25. GALVESTON, TX: 75,653 pounds

26. ALLEN, IN: 69,437 pounds
27. MIDDLESEX, NJ: 64,095 pounds
28. OSCEOLA, MI: 60,700 pounds
29. LORAIN, OH: 59,994 pounds
30. TARRANT, TX: 58,684 pounds
31. CALCASIEU, LA: 56,663 pounds
32. SCHENECTADY, NY: 56,405 pounds
33. LAUDERDALE, TN: 55,550 pounds
34. NUECES, TX: 55,457 pounds
35. SUMTER, GA: 53,769 pounds
36. PONTOTOC, OK: 52,896 pounds
37. MULTNOMAH, OR: 49,182 pounds
38. UNION, OH: 49,100 pounds
39. BROOKE, WV: 48,769 pounds
40. EAST BATON ROUGE, LA: 46,661 pounds
41. SUMNER, TN: 46,252 pounds
42. VERNON, MO: 44,700 pounds
43. POSEY, IN: 43,832 pounds
44. JACKSON, MS: 43,741 pounds
45. MCLEAN, IL: 42,409 pounds
46. MONROE, MI: 42,000 pounds
47. MAURY, TN: 41,280 pounds
48. INGHAM, MI: 41,266 pounds
49. MERCER, OH: 41,180 pounds
50. MORGAN, AL: 40,740 pounds
51. NORTHUMBERLAND, PA: 40,736 pounds
52. MOBILE, AL: 40,283 pounds
53. PRICE, WI: 40,251 pounds
54. WOODFORD, KY: 39,793 pounds
55. HARVEY, KS: 39,359 pounds
56. ALLEGAN, MI: 39,345 pounds
57. BAY, FL: 38,030 pounds
58. SANDUSKY, OH: 37,143 pounds

59. ROBERTSON, TN: 36,880 pounds
60. IBERVILLE, LA: 36,405 pounds
61. TIPPECANOE, IN: 36,332 pounds
62. AUGLAIZE, OH: 36,012 pounds
63. ST. CHARLES, LA: 35,505 pounds
64. PANOLA, MS: 35,358 pounds
65. MARION, AL: 35,015 pounds
66. HARDY, WV: 34,966 pounds
67. UNION, AR: 34,179 pounds
68. ECTOR, TX: 33,757 pounds
69. MIDLAND, MI: 33,008 pounds
70. ALLEGHENY, PA: 32,747 pounds
71. TRUMBULL, OH: 32,484 pounds
72. NEW CASTLE, DE: 31,705 pounds
73. GRENADA, MS: 31,400 pounds
74. JACKSON, AL: 31,321 pounds
75. FOUNTAIN, IN: 30,844 pounds
76. MADISON, IL: 30,262 pounds
77. LABETTE, KS: 30,000 pounds
78. ROCK ISLAND, IL: 29,984 pounds
79. SPALDING, GA: 28,900 pounds
80. LEE, MS: 28,440 pounds
81. WASHINGTON, AL: 28,228 pounds
82. BROWN, OH: 28,088 pounds
83. LOGAN, OH: 27,600 pounds
84. BARRY, MO: 27,215 pounds
85. LAKE, IN: 27,197 pounds
86. DUBOIS, IN: 26,839 pounds
87. TUSCARAWAS, OH: 25,258 pounds
88. SEBASTIAN, AR: 25,250 pounds
89. DUBUQUE, IA: 25,000 pounds
90. LOS ANGELES, CA: 24,956 pounds
91. ST. CROIX, VI: 24,824 pounds

92. LAWRENCE, TN: 24,200 pounds
93. MCKINLEY, NM: 24,113 pounds
94. GUAYAMA, PR: 23,801 pounds
95. MCPHERSON, KS: 23,709 pounds
96. LEE, IA: 23,496 pounds
97. UNION, NJ: 23,451 pounds
98. PEORIA, IL: 23,110 pounds
99. CLARK, IN: 23,089 pounds
100. DE KALB, IN: 23,035 pounds

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Zip Codes with Reported Total Environmental Releases

of ETHYLBENZENE (100-41-4) from the About The Chemicals section of Scorecard

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Ranked by (select your ranking criteria)

Total environmental releases

in

Entire United States Go (explain)

1. 77530 (TX): 929,285 pounds
2. 64119 (MO): 297,000 pounds
3. 63042 (MO): 161,136 pounds
4. 49508 (MI): 147,000 pounds
5. 39701 (MS): 126,000 pounds
6. 48439 (MI): 114,427 pounds
7. 03874 (NH): 109,652 pounds
8. 23523 (VA): 108,733 pounds
9. 40213 (KY): 92,033 pounds
10. 55116 (MN): 91,600 pounds
11. 30360 (GA): 90,824 pounds
12. 73134 (OK): 85,800 pounds
13. 77541 (TX): 82,672 pounds
14. 71129 (LA): 81,984 pounds
15. 63385 (MO): 76,900 pounds
16. 48184 (MI): 71,581 pounds
17. 43610 (OH): 70,700 pounds
18. 48121 (MI): 70,128 pounds
19. 48317 (MI): 68,630 pounds
20. 77017 (TX): 66,323 pounds
21. 30354 (GA): 65,340 pounds
22. 49631 (MI): 60,700 pounds
23. 60633 (IL): 60,024 pounds
24. 44012 (OH): 58,600 pounds
25. 38063 (TN): 55,550 pounds

26. 77701 (TX): 55,438 pounds
27. 08818 (NJ): 54,945 pounds
28. 21224 (MD): 54,681 pounds
29. 31709 (GA): 53,769 pounds
30. 74820 (OK): 52,896 pounds
31. 46783 (IN): 52,600 pounds
32. 43040 (OH): 49,100 pounds
33. 26062 (WV): 48,359 pounds
34. 12150 (NY): 47,105 pounds
35. 37066 (TN): 46,252 pounds
36. 77590 (TX): 45,477 pounds
37. 70601 (LA): 45,431 pounds
38. 60131 (IL): 45,223 pounds
39. 70805 (LA): 45,022 pounds
40. 64772 (MO): 44,700 pounds
41. 47620 (IN): 43,832 pounds
42. 39581 (MS): 43,741 pounds
43. 66115 (KS): 43,000 pounds
44. 61761 (IL): 42,409 pounds
45. 76010 (TX): 41,300 pounds
46. 37174 (TN): 41,280 pounds
47. 45822 (OH): 41,180 pounds
48. 48160 (MI): 41,000 pounds
49. 35601 (AL): 40,740 pounds
50. 17857 (PA): 40,736 pounds
51. 54555 (WI): 40,251 pounds
52. 40383 (KY): 39,793 pounds
53. 49423 (MI): 39,355 pounds
54. 32401 (FL): 38,030 pounds
55. 97210 (OR): 37,447 pounds
56. 37172 (TN): 36,880 pounds
57. 48901 (MI): 36,600 pounds
58. 47905 (IN): 36,332 pounds

59. 48211 (MI): 36,044 pounds
60. 45885 (OH): 36,012 pounds
61. 40241 (KY): 35,600 pounds
62. 66111 (KS): 35,554 pounds
63. 38606 (MS): 35,358 pounds
64. 35563 (AL): 35,015 pounds
65. 26836 (WV): 34,966 pounds
66. 71730 (AR): 34,179 pounds
67. 79766 (TX): 33,676 pounds
68. 38901 (MS): 31,400 pounds
69. 35768 (AL): 31,321 pounds
70. 48667 (MI): 31,000 pounds
71. 47987 (IN): 30,844 pounds
72. 48134 (MI): 30,794 pounds
73. 48359 (MI): 30,011 pounds
74. 67357 (KS): 30,000 pounds
75. 77592 (TX): 29,926 pounds
76. 70721 (LA): 29,830 pounds
77. 30223 (GA): 28,900 pounds
78. 38802 (MS): 28,440 pounds
79. 36553 (AL): 28,228 pounds
80. 62084 (IL): 28,100 pounds
81. 45154 (OH): 28,088 pounds
82. 77651 (TX): 28,064 pounds
83. 36652 (AL): 28,058 pounds
84. 70047 (LA): 27,713 pounds
85. 43319 (OH): 27,600 pounds
86. 44481 (OH): 27,486 pounds
87. 65708 (MO): 27,215 pounds
88. 48091 (MI): 25,501 pounds
89. 44622 (OH): 25,258 pounds
90. 72908 (AR): 25,250 pounds
91. 52004 (IA): 25,000 pounds

92. 00851 (VI): 24,824 pounds
93. 61244 (IL): 24,471 pounds
94. 38464 (TN): 24,200 pounds
95. 87347 (NM): 24,113 pounds
96. 67062 (KS): 24,000 pounds
97. 00784 (PR): 23,801 pounds
98. 67460 (KS): 23,709 pounds
99. 52627 (IA): 23,496 pounds
100. 48341 (MI): 23,346 pounds

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Facilities with Reported Total Environmental Releases

of ETHYLBENZENE (100-41-4) from the About the Chemicals section of Scorecard

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Ranked by (select your ranking criteria)

Total environmental releases
in
Entire United States
from
All reporting sectors
Go (explain)

1. LYONDELL CHEMICAL WORLDWIDE INC., CHANNELVIEW, TX: 918,528 Pounds
2. FORD MOTOR CO., KANSAS CITY ASSEMBLY PLANT, CLAYCOMO, MO: 297,000 Pounds
3. FORD MOTOR CO. ST. LOUIS ASSEMBLY, HAZELWOOD, MO: 161,000 Pounds
4. SANDERSON PLUMBING PRODS. INC., COLUMBUS, MS: 126,000 Pounds
5. VEMCO INC., GRAND BLANC, MI: 114,427 Pounds
6. VENTURE HOLDINGS CORP. BAILEY CORP., SEABROOK, NH: 108,324 Pounds
7. FORD MOTOR CO. NORFOLK ASSEMBLY PLANT, NORFOLK, VA: 93,000 Pounds
8. FORD MOTOR CO., LOUISVILLE ASSEMBLY PLANT, LOUISVILLE, KY: 92,033 Pounds
9. FORD MOTOR CO. - TWIN CITIES ASSEMBLY PLANT, SAINT PAUL, MN: 91,600 Pounds
10. GM MLCG - DORAVILLE ASSEMBLY, DORAVILLE, GA: 90,500 Pounds
11. GM SCG, OKLAHOMA CITY ASSEMBLY, OKLAHOMA CITY, OK: 85,800 Pounds
12. STEELCASE INC., GRAND RAPIDS, MI: 83,000 Pounds
13. GMTG - Shreveport Assembly, SHREVEPORT, LA: 81,520 Pounds
14. DOW CHEMICAL CO. FREEPORT TEXAS, FREEPORT, TX: 80,709 Pounds
15. GMTG WENTZILLE TRUCK ASSEMBLY, WENTZVILLE, MO: 76,900 Pounds
16. TOLEDO ASSEMBLY PLANT I, TOLEDO, OH: 70,700 Pounds
17. FORD MOTOR CO. DEARBORN ASSEMBLY PLANT, DEARBORN, MI: 70,100

Pounds

18. FORD MOTOR CO. UTICA PLANT, SHELBY TOWNSHIP, MI: 68,630 Pounds
19. LYONDELL-CITGO REFINING CO. LTD., HOUSTON, TX: 66,323 Pounds
20. FORD MOTOR CO. ATLANTA ASSEMBLY PLANT, HAPEVILLE, GA: 65,340 Pounds
21. STEELCASE INC., KENTWOOD, MI: 64,000 Pounds
22. TEXTRON AUTOMOTIVE CO. - EVART PLANT, EVART, MI: 60,700 Pounds
23. FORD MOTOR CO., CHICAGO ASSEMBLY PLANT, CHICAGO, IL: 60,024 Pounds
24. FORD MOTOR CO. OHIO ASSEMBLY PLANT, AVON LAKE, OH: 58,600 Pounds
25. TENNESSEE ELECTROPLATING, RIPLEY, TN: 55,550 Pounds
26. GMC NORTH AMERICAN TRUCK GROUP, BALTIMORE, MD: 54,062 Pounds
27. FORD EDISON ASSEMBLY PLANT, EDISON, NJ: 54,000 Pounds
28. TEXTRON AUTOMOTIVE CO., AMERICUS, GA: 53,769 Pounds
29. FORD MOTOR CO. - WAYNE ASSEMBLY PLANT, WAYNE, MI: 53,280 Pounds
30. CAMROSE TECH. NOLOGIES L.L.C., ADA, OK: 52,896 Pounds
31. GMTG FORT WAYNE ASSEMBLY, FORT WAYNE, IN: 52,600 Pounds
32. HONDA OF AMERICA MFG. INC., MARYSVILLE, OH: 47,600 Pounds
33. SCHENECTADY INTL. INC., ROTTERDAM JUNCTION, NY: 47,105 Pounds
34. GF OFFICE FURNITURE L.PT., GALLATIN, TN: 46,252 Pounds
35. BMAT MDD INC., FRANKLIN PARK, IL: 45,223 Pounds
36. 3M NEVADA PLANT, NEVADA, MO: 44,700 Pounds
37. CITGO PETROLEUM CORP., LAKE CHARLES, LA: 43,556 Pounds
38. MITSUBISHI MOTOR MFG. OF AMERICA INC., NORMAL, IL: 42,409 Pounds
39. GM MLCG-FAIRFAX ASSEMBLY, KANSAS CITY, KS: 42,250 Pounds
40. GMC TRUCK GROUP ARLINGTON ASSEMBLY PLANT, ARLINGTON, TX: 41,300 Pounds
41. SATURN CORP., SPRING HILL, TN: 41,280 Pounds
42. HUFFY BICYCLE CO., CELINA, OH: 41,180 Pounds
43. FORD MOTOR CO., MILAN PLASTICS PLANT, MILAN, MI: 41,000 Pounds
44. RESILITE SPORTS PRODS. INC., NORTHUMBERLAND, PA: 40,736 Pounds
45. GEORGIA PACIFIC CORP., PHILLIPS, WI: 40,251 Pounds
46. OSRAM SYLVANIA PRODS. INC., VERSAILLES, KY: 39,793 Pounds

47. GENERAL ELECTRIC PLASTICS CO., MOUNT VERNON, IN: 39,255 Pounds
48. AFCO INDS. INC., HOLLAND, MI: 39,200 Pounds
49. MOBIL OIL BEAUMONT REFY., BEAUMONT, TX: 39,000 Pounds
50. ARIZONA CHEMICAL CO., PANAMA CITY, FL: 38,030 Pounds
51. AMOCO CHEMICAL CO., DECATUR, AL: 38,000 Pounds
52. GM LANSING PLANTS 2 3 & 6 (BODY), LANSING, MI: 36,600 Pounds
53. GM MLCG - Hamtramck Assembly, DETROIT, MI: 36,044 Pounds
54. GOODYEAR TIRE & RUBBER CO., SAINT MARYS, OH: 36,012 Pounds
55. FORD MOTOR CO., KENTUCKY TRUCK PLANT, LOUISVILLE, KY: 35,600 Pounds
56. BATESVILLE CASKET CO. INC., BATESVILLE, MS: 35,358 Pounds
57. STERLING CHEMICALS INC., TEXAS CITY, TX: 35,192 Pounds
58. 3M, GUIN, AL: 35,015 Pounds
59. AMERICAN WOODMARK CORP., MOOREFIELD, WV: 34,966 Pounds
60. SOMMER ALLIBERT IND. INC., KANSAS CITY, KS: 34,964 Pounds
61. GUNDERSON INC., PORTLAND, OR: 34,238 Pounds
62. EXXON CO. USA BATON ROUGE REFY., BATON ROUGE, LA: 33,075 Pounds
63. HEATCRAFT INC., GRENADA, MS: 31,400 Pounds
64. LOZIER CORP., SCOTTSBORO, AL: 31,321 Pounds
65. DOW CHEMICAL CO. - MIDLAND OPS., MIDLAND, MI: 31,000 Pounds
66. MASTER GUARD CORP., VEEDERSBURG, IN: 30,844 Pounds
67. AUTOALLIANCE INTL. INC., FLAT ROCK, MI: 30,794 Pounds
68. GM MCG - ORION ASSEMBLY, ORION, MI: 30,011 Pounds
69. A. O. SMITH ENGINEERED STORAGE PRODS. CO. (BOLTED), PARSONS, KS: 30,000 Pounds
70. STANDARD PRODS. CO., GRIFFIN, GA: 28,900 Pounds
71. CIBA SPECIALTY CHEMICALS CORP., MC INTOSH, AL: 28,228 Pounds
72. COS-MAR CO., CARVILLE, LA: 28,113 Pounds
73. EQUILON WOOD RIVER REFINING CO., ROXANA, IL: 28,100 Pounds
74. TRINTY IND. INC. PLANT 101, MOUNT ORAB, OH: 28,088 Pounds
75. HUNTSMAN CORP. - C4/O&O PLANT, PORT NECHES, TX: 28,000 Pounds
76. ATLANTIC MARINE INC., MOBILE, AL: 27,931 Pounds
77. MOTIVA NORCO REFINING CO., NORCO, LA: 27,713 Pounds
78. HONDA OF AMERICA MFG. INC., EAST LIBERTY, OH: 27,600 Pounds

79. GM SCG LORDSTOWN ASSEMBLY, LORDSTOWN, OH: 27,400 Pounds
80. EFCO CORP., MONETT, MO: 27,215 Pounds
81. U.S. CAN CO. PLANT #20 WEIRTON, WEIRTON, WV: 27,185 Pounds
82. CHEVRON PRODS. CO., PASCAGOULA REFY., PASCAGOULA, MS: 26,517 Pounds
83. CHRYSLER CORP., WARREN TRUCK ASSEMBLY PLANT 1, WARREN, MI: 25,500 Pounds
84. WHIRLPOOL CORP., FORT SMITH, AR: 25,250 Pounds
85. JOHN DEERE DUBUQUE WORKS, DUBUQUE, IA: 25,000 Pounds
86. HOVENSA L.L.C., CHRISTIANSTED, VI: 24,824 Pounds
87. HUNTSMAN POLYMERS CORP., ODESSA, TX: 24,776 Pounds
88. COMMERCIAL & ARCHITECTURAL PRODS. INC. MARLITE (DBA), DOVER, OH: 24,753 Pounds
89. MURRAY INC., LAWRENCEBURG, TN: 24,200 Pounds
90. GIANT REFINING CO., JAMESTOWN, NM: 24,113 Pounds
91. HAY & FORAGE IND., HESSTON, KS: 24,000 Pounds
92. PHILLIPS PUERTO RICO CORE INC., GUAYAMA, PR: 23,801 Pounds
93. NATL. COOP. REFY. ASSOC., MC PHERSON, KS: 23,709 Pounds
94. WABASH NATL. CORP., FRUEHAUF DIV., FORT MADISON, IA: 23,250 Pounds
95. CATERPILLAR INC., MOSSVILLE COMPLEX, MOSSVILLE, IL: 23,110 Pounds
96. COOPER TIRE & RUBBER CO. ENGINEERED PRODS. DIV., AUBURN, IN: 23,035 Pounds
97. KITCHEN KOMPACT, JEFFERSONVILLE, IN: 23,000 Pounds
98. WASTEQUIP MFG. CO. MAYFAB DIV., BEEVILLE, TX: 22,931 Pounds
99. WASTEQUIP INC., BROOKHAVEN, MS: 22,832 Pounds
100. PHILLIPS 66 CO., BORGER, TX: 22,781 Pounds

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Industrial Sectors with Reported Total Environmental Releases

of ETHYLBENZENE (100-41-4) by Industrial Sector (2-digit SIC) from the About the Chemicals section of Scorecard

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Ranked by (select your ranking criteria)

Total environmental releases

in

Entire United States Go (explain)

1. 37: Transportation Equipment : 3,223,379 pounds
2. 28: Chemicals And Allied Products : 1,997,166 pounds
3. 29: Petroleum And Coal Products : 986,560 pounds
4. 34: Fabricated Metal Products : 626,081 pounds
5. 24: Lumber And Wood Products : 576,585 pounds
6. 30: Rubber And Misc. Plastics Products : 476,106 pounds
7. 25: Furniture And Fixtures : 400,004 pounds
8. 35: Industrial Machinery And Equipment : 295,653 pounds
9. 36: Electronic & Other Electric Equipment : 202,644 pounds
10. 33: Primary Metal Industries : 166,353 pounds
11. 51: Wholesale Trade--Nondurable Goods : 122,301 pounds
12. 39: Miscellaneous Manufacturing Industries : 97,043 pounds
13. 32: Stone, Clay, And Glass Products : 39,496 pounds
14. 26: Paper And Allied Products : 29,095 pounds
15. 27: Printing And Publishing : 20,064 pounds
16. 49: Electric, Gas, And Sanitary Services : 17,464 pounds
17. 20: Food And Kindred Products : 11,950 pounds
18. 13: Oil And Gas Extraction : 8,505 pounds
19. NA: Not reported : 6,487 pounds
20. 38: Instruments And Related Products : 3,310 pounds
21. 73: Business Services : 1,102 pounds
22. 23: Apparel And Other Textile Products : 961 pounds
23. 87: Engineering & Management Services : 258 pounds
24. 95: Environmental Quality And Housing : 5 pounds

25. 44: Water Transportation : 1 pounds

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Regulatory Coverage

of ETHYLBENZENE (100-41-4) from Scorecard

Federal Regulatory Program Lists

- Air Contaminants (Occupational and Safety Health Act)
- Hazardous Air Pollutants (Clean Air Act)
- Hazardous Substances (Superfund)
- Maximum Contaminant Levels (Safe Drinking Water Act)
- Priority Pollutants (Clean Water Act)
- Toxic Release Inventory Chemicals

California State Regulatory Program Lists

- California Air Toxics "Hot Spots" Chemicals (Assembly Bill 2588)
- California Toxic Air Contaminants (Assembly Bill 1807)
- Maximum Contaminant Levels (California Safe Drinking Water Act)

Environmental Hazard Lists

- Dangerous for the Environment (Nordic Council of Ministers)

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Basic Testing to Identify Chemical Hazards

for ETHYLBENZENE (100-41-4) from Scorecard

The U.S. EPA conducted a comprehensive review of publicly available chemical testing data in 1997 to examine whether the basic information needed to identify chemical hazards is available for high production volume chemicals. EPA searched major chemical databases to determine if the following tests had been conducted on a chemical:

- Acute toxicity
- Chronic toxicity
- Neurotoxicity
- Developmental or reproductive toxicity
- Mutagenicity
- Carcinogenicity
- Ecotoxicity
- Environmental fate

Eight basic tests to identify chemical hazards have been conducted and are publicly available for this chemical.

More on the importance of basic toxicity testing

Reference

EPA. Chemical Hazard Data Availability Study: High Production Volume (HPV) Chemicals and SIDS Testing
Office of Pollution Prevention and Toxics, EPA,Washington, DC. 1998.

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Safety Assessment Data

for ETHYLBENZENE (100-41-4) from Scorecard

Are Risk Assessment Values Available?

Health Risk of Concern	Inhalation	Ingestion
Cancer	Not a recognized carcinogen	Not a recognized carcinogen
Noncancer	Yes	Yes

Are Exposure Data Available?

Type of Exposure	
Inhalation - ambient air	Monitoring data available in some states
Inhalation - indoor air	Yes
Ingestion	Yes

- See the data US EPA possesses for safety assessment.

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Scorecard Risk Characterization Data

for ETHYLBENZENE (100-41-4) from Scorecard

Risk Assessment Values or Standards

	Value	Units	Reference
Inhalation cancer risk value (potency)	Not a recognized or suspect carcinogen		
Inhalation noncancer risk value (reference concentration)	2000	ug/m3	OEHHA2000-REL
National ambient air quality standard	Gap in regulatory coverage		
Ingestion cancer risk value (potency)	Not a recognized or suspect carcinogen		
Ingestion noncancer risk value (reference dose)	0.1	mg/kg-day	IRIS-HEAST
National water quality standard	0.7	mg/L	SDWA-MCL

See the data US EPA possesses for safety assessment.

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Chemical Classes

for ETHYLBENZENE (100-41-4) from Scorecard

Note that ETHYLBENZENE may be a member of the following classes:

- VOLATILE ORGANIC COMPOUNDS

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Agency for Toxic Substances and Disease Registry

Public Health Statement

Ethylbenzene

ATSDR Public Health Statement, December 1990

This Statement was prepared to give you information about ethylbenzene and to emphasize the human health effects that may result from exposure to it. The Environmental Protection Agency (EPA) has identified 1,177 sites on its National Priorities List (NPL). Ethylbenzene has been found at 227 of these sites. However, we do not know how many of the 1,177 NPL sites have been evaluated for ethylbenzene. As EPA evaluates more sites, the number of sites at which ethylbenzene is found may change. The information is important for you because ethylbenzene may cause harmful health effects and because these sites are potential or actual sources of human exposure to ethylbenzene.

When a chemical is released from a large area, such as an industrial plant, or from a container, such as a drum or bottle, it enters the environment as a chemical emission. This emission, which is also called a release, does not always lead to exposure. You can be exposed to a chemical only when you come into contact with the chemical. You may be exposed to it in the environment by breathing, eating, or drinking substances containing the chemical or from skin contact with it.

If you are exposed to a hazardous substance such as ethylbenzene, several factors will determine whether harmful health effects will occur and what the type and severity of those health effects will be. These factors include the dose (how much), the duration (how long), the route or pathway by which you are exposed (breathing, eating, drinking, or skin contact), the other chemicals to which you are exposed, and your individual characteristics such as age, sex, nutritional status, family traits, life style, and state of health.

What is ethylbenzene?

Ethylbenzene is a colorless liquid that smells like gasoline. It evaporates at room temperature and burns easily. Ethylbenzene occurs naturally in coal tar and petroleum. It is also found in many man-made products, including paints, inks, and insecticides. Gasoline contains about 2% (by weight) ethylbenzene. It is most commonly found as a vapor in the air. This is because ethylbenzene moves easily into the air from water and soil. Once in the air, other chemicals help break down ethylbenzene into chemicals found in smog. This breakdown happens in about 3 days with the aid of sunlight. In surface water such as rivers

and harbors, ethylbenzene breaks down by reacting with other compounds naturally present in the water. In soil, the major way ethylbenzene is broken down is by soil bacteria. It can also move very quickly into groundwater, since it does not readily bind to soil. Near hazardous waste sites, the levels of ethylbenzene in the air, water, and soil could be much higher than in other areas.

How might I be exposed to ethylbenzene?

There are a variety of ways you may be exposed to this chemical. If you live in a highly populated area or near many factories or heavily traveled highways, you may be exposed to ethylbenzene in the air. Releases of ethylbenzene into these areas occur from burning oil, gas, and coal and from discharges of ethylbenzene from some types of factories. The median level of ethylbenzene in city air is about 0.62 parts of ethylbenzene per billion parts (ppb) of air. The median level in suburban air is about 0.62 ppb. In contrast, the median level of ethylbenzene measured in air in country locations is about 0.01 ppb. Indoor air has a higher median concentration of ethylbenzene (about 1 ppb) than outdoor air. This is because ethylbenzene builds up after you use household products such as cleaning products or paints.

Ethylbenzene was found in only 1 out of 10 of the United States rivers and streams tested in 1982 and 1983. The average level measured was 5.0 ppb. Ethylbenzene gets into water from factory releases, boat fuel, and poor disposal of waste. Background levels in soils have not been reported. Ethylbenzene may get into the soil by gasoline or other fuel spills and poor disposal of industrial and household wastes.

Some people are exposed to ethylbenzene in the workplace. Gas and oil workers may come into contact with ethylbenzene either through the skin or by breathing ethylbenzene vapors. Varnish workers, spray painters and persons involved in gluing operations may also be exposed to high levels of ethylbenzene. Exposure may also occur in factories that use ethylbenzene to produce other chemicals. Families of these workers may be exposed to ethylbenzene through contact with contaminated clothing.

You may be exposed to ethylbenzene if you live near hazardous waste sites containing ethylbenzene or areas where ethylbenzene spills have occurred. Higher than background levels of ethylbenzene were detected in groundwater near a landfill and near an area where a fuel spill had occurred. No specific information on human exposure to ethylbenzene near hazardous waste sites is available.

You may also be exposed to ethylbenzene from the use of many consumer products. Gasoline is a common source of ethylbenzene exposure. Other sources of ethylbenzene exposure come from the use of this chemical as a solvent in pesticides, carpet glues, varnishes and paints, and from the use of tobacco products. Ethylbenzene does not generally build up in food. However, some vegetables may contain very small amounts of it.

How can ethylbenzene enter and leave my body?

When you breathe air containing ethylbenzene vapor, it enters your body rapidly and almost completely through your lungs. Ethylbenzene in food or water can also rapidly and almost completely enter your body through the digestive tract. It may enter through your skin when you come into contact with liquids containing ethylbenzene. Ethylbenzene vapors do not enter through your skin to any large degree. People living in urban areas or in areas near hazardous waste sites may be exposed by breathing air or by drinking water contaminated with ethylbenzene.

Once in your body, ethylbenzene is broken down into other chemicals. Most of it leaves in the urine within 2 days. Small amounts can also leave through the lungs and in feces. Liquid ethylbenzene also enters through your skin and is broken down. Ethylbenzene in high levels is broken down slower in your body than low levels of ethylbenzene. Similarly, ethylbenzene mixed with other solvents is also broken down more slowly than ethylbenzene alone. This slower breakdown may increase the time it takes for ethylbenzene to leave your body.

How can ethylbenzene affect my health?

At certain levels, exposure to ethylbenzene can harm your health. People exposed to low levels of ethylbenzene in the air for short periods of time have complained of eye and throat irritation. Persons exposed to higher levels have shown signs of more severe effects such as decreased movement and dizziness. No studies have reported death in humans following exposure to ethylbenzene. However, evidence from animals suggests that it can cause death at very high concentrations. Whether or not long-term exposure to ethylbenzene affects human health is not known because little information is available. Short-term exposure of laboratory animals to high concentrations of ethylbenzene in air may cause liver and kidney damage, nervous system changes, and blood changes. The link between these health effects and exposure to ethylbenzene is not clear because of conflicting results and weaknesses in many of the studies.

Also, there is no clear evidence that the ability to get pregnant is affected by breathing air, drinking water containing ethylbenzene, or coming into direct contact with ethylbenzene through the skin. Birth defects have occurred in newborn animals whose mothers were exposed by breathing air contaminated with ethylbenzene. The seriousness of these effects seems to increase with higher exposure levels. One long-term study in animals suggests that ethylbenzene may cause tumors. However, this study had many weaknesses and no conclusions could be drawn about possible cancer effects in humans. EPA has determined that ethylbenzene is not classifiable as to human carcinogenicity.

What levels of exposure have resulted in harmful health effects?

Low levels of ethylbenzene in the air may cause harmful health effects. More serious effects to your health may occur at higher levels. You can smell ethylbenzene in the air at concentrations as low as 2 parts of ethylbenzene per million parts of air by volume (ppm).

There are no reliable data on the effects in humans after eating, drinking, or breathing ethylbenzene or following direct exposure to the skin. For this reason, levels of exposure that may affect your health are estimated from animal studies. Only two reports described the results of eye or skin exposure to ethylbenzene. In these studies, liquid ethylbenzene caused eye damage and skin irritation in rabbits. More animal studies are available that describe the effects of breathing air or drinking water containing ethylbenzene. Tables 1-1, 1-2, 1-3, and 1-4 show the relationship between exposure to ethylbenzene in air, food, or water and known health effects.

A Minimal Risk Level (MRL) is also included in Table 1-1. This MRL was derived from animal data for

long-term exposure. The MRL provides a basis for comparison with levels that people might encounter either in the air, in food, or in drinking water. If a person is exposed to ethylbenzene at an amount below the MRL, it is not expected that harmful (noncancer) health effects will occur. Because this level is based only on information currently available, some uncertainty is always associated with it. Also, because the method for deriving MRLs does not use any information about cancer, an MRL does not imply anything about the presence, absence, or level of risk for cancer.

Is there a medical test to determine whether I have been exposed to ethylbenzene?

Ethylbenzene is found in the blood, urine, breath, and some body tissues of exposed persons. Urine is most commonly tested to determine exposure to ethylbenzene. The test measures the presence of substances formed following an exposure to ethylbenzene. These substances are formed by the breakdown of ethylbenzene. You should have this test done within a few hours after exposure occurs, because these substances leave the body very quickly. Although this test can prove your exposure to ethylbenzene, it cannot yet predict the kind of health effects that might develop from that exposure.

What recommendations has the federal government made to protect human health?

The federal government has formed regulatory standards and guidelines to protect you from possible health effects of ethylbenzene in the environment. EPA's Office of Drinking Water (ODW) recommends 680 ppb (0.68 mg/L) as the acceptable exposure concentration of ethylbenzene in drinking water for an average weight adult. This value is for lifetime exposure and is not expected to increase the chance of experiencing (noncancer) health effects. The same EPA office (ODW) recommends higher acceptable levels of ethylbenzene in water for shorter periods (32,000 ppb or 32 mg/L for 1 day, 3,200 ppb or 3.2 mg/L for 10 days). These levels are stated to be acceptable for small children. EPA also recommends that if you eat fish and drink water from a body of water, the water should contain no more than 1.4 mg ethylbenzene/L.

EPA requires that a release of 1,000 pounds or more of ethylbenzene be reported to the Federal Government National Response Center in Washington, D.C.

The Occupational Safety and Health Administration (OSHA) set a legal limit of 100 ppm ethylbenzene in air. This is for exposure at work for 8 hours per day. OSHA also set a limit of 125 ppm for a 15-minute period.

The National Institute for Occupational Safety and Health (NIOSH) also recommends an exposure limit for ethylbenzene of 100 ppm. This is for exposure to ethylbenzene in air at work for up to 10 hours per day in a 40-hour work week. NIOSH classifies ethylbenzene exposures of 2,000 ppm in air as immediately dangerous to life or health.

Where can I get more information?

If you have any more questions or concerns not covered here, please contact your state health or environmental department or:

Agency for Toxic Substances and Disease Registry
Division of Toxicology
1600 Clifton Road, E-29
Atlanta, Georgia 30333

This agency can also give you information on the location of the nearest occupational and environmental health clinics. Such clinics specialize in recognizing, evaluating, and treating illnesses that result from exposure to hazardous substances.

ETHYL BENZENE

Ethyl benzene is a federal hazardous air pollutant and was identified as a toxic air contaminant in April 1993 under AB 2728.

CAS Registry Number: 100-41-4

Molecular Formula: C_8H_{10}

Description

Ethyl benzene is a colorless, flammable liquid with an aromatic odor. It is practically insoluble in water and is soluble in alcohol, carbon tetrachloride, ether, and other organic solvents. Ethyl benzene evaporates about 94 times more slowly than ether (HSDB, 1991).

Physical Properties of Ethyl benzene

Molecular Weight	106.16
Boiling Point	136.2 oC
Melting Point	-94.97 oC
Flash Point	18 oC (closed cup)
Vapor Density	3.66 (air = 1)
Vapor Pressure	9.53 mm Hg at 25 oC
Density/Specific Gravity	0.867 at 20/4 oC (water = 1)
Log Octanol/Water Partition Coefficient	3.15
Conversion Factor	1 ppm = 4.34 mg/m3

(Howard, 1990; HSDB, 1991; Merck, 1989; Sax, 1987; U.S. EPA, 1994a)

SOURCES AND EMISSIONS

A. Sources

Ethyl benzene is used as an intermediate in the production of styrene and as a solvent in paint and other consumer products. Ethyl benzene is also used in petroleum refining. Ethyl benzene has been detected in auto emissions and cigarette smoke (Howard, 1990).

The primary stationary sources that have reported emissions of ethyl benzene in California are manufacturers of aircraft and parts, petroleum refining, and manufacturers of miscellaneous plastics products (ARB, 1997b). Ethyl benzene has also been detected but not quantified in motor vehicle exhaust by the Air Resources Board (ARB) (ARB, 1995e).

B. Emissions

The total emissions of ethyl benzene from stationary sources in California are estimated to be at least 140,000 pounds per year, based on data reported under the Air Toxics "Hot Spots" Program (AB 2588) (ARB, 1997b).

C. Natural Occurrence

Ethyl benzene is a component of crude oil (HSDB, 1991).

AMBIENT CONCENTRATIONS

Ethyl benzene is routinely monitored by the statewide ARB air toxics network. The network's mean concentration of ethyl benzene from January 1996 through December 1996 is estimated to be 1.61 micrograms per cubic meter (µg/m3) or 0.37 parts per billion (ppb) (ARB, 1997c).

The United States Environmental Protection Agency (U.S. EPA) has also compiled ambient concentration data from several studies throughout the United States. Data from 11 United States cities during 1990 reported an overall mean concentration of 1.68 µg/m3 (0.39 ppb) (U.S. EPA, 1993a).

INDOOR SOURCES AND CONCENTRATIONS

Ethyl benzene is a chemical solvent found in many consumer products such as paint and cleaning products. However, ethyl benzene comprises less than 10 percent by weight of the product ingredients in these products (Sack and Steele, 1989).

Ethyl benzene was measured in Los Angeles homes during winter and summer seasons in the 1987 Total Exposure Assessment Methodology study (Pellizzari et al., 1989). The mean indoor concentrations of ethyl benzene were 5.02 to 6.64 µg/m3 and 2.48 to 3.03 µg/m3 for winter and summer, respectively. In contrast, the mean outdoor concentrations of ethyl benzene were 4.58 µg/m3 and 1.61 µg/m3 for winter and summer, respectively.

In a study of east coast public buildings, the average indoor concentrations of ethyl benzene ranged from 3.6 to 6.8 µg/m3 (Sheldon et al, 1988a). In other public buildings, the mean concentrations of ethyl benzene for most of the indoor environments ranged from 1.01 to 10.15 µg/m3 except for a new office with a high mean concentration of 51.26 µg/m3 (Sheldon et al, 1988b).

Studies in Raleigh, North Carolina and Boston, Massachusetts measured average in-vehicle concentrations of ethyl benzene of 5.8 µg/m3 and 8.8 µg/m3 and maximum concentrations of 21.6 µg/m3 and 21.8 µg/m3, respectively; about 3 to 5 times greater than what was measured in the ambient air (Chan et al., 1991a; Chan et al., 1991b).

ATMOSPHERIC PERSISTENCE

The only important chemical loss process for ethyl benzene in the troposphere is by the reaction with the hydroxyl (OH) radical. The calculated half-life and lifetime of ethyl benzene due to reaction with the OH radical are 1.4 days and 2.0 days, respectively. The reaction products are expected to include ethylphenols, acetophenone, glyoxal, ethylglyoxal, and other ring-opened products (Atkinson, 1995). Its reaction products include glyoxal, ethylglyoxal, acetophenone, formaldehyde, and acetaldehyde (Kao, 1994).

AB 2588 RISK ASSESSMENT INFORMATION

Although ethyl benzene is reported as being emitted in California from stationary sources no health values (cancer or non-cancer) are listed in the California Air Pollution Control Officers Association Air Toxics "Hot Spots" Program Revised 1992 Risk Assessment Guidelines for use in risk assessments (CAPCOA, 1993).

HEALTH EFFECTS

Probable routes of human exposure to ethyl benzene are inhalation and ingestion (HSDB, 1991).

Non-Cancer: Ethyl benzene is a central nervous system depressant at high levels of exposure. Ethyl benzene is also irritating to the eyes and respiratory tract. Animal studies have shown effects on the blood, liver and kidneys from chronic inhalation exposure to ethyl benzene (U.S. EPA, 1994a). Persons with existing skin disorders, liver, kidney, nervous system, blood and hemopoietic-organ disorders, and women with ovulation and menstrual cycle disorders may be more susceptible to adverse effects (HSDB, 1991).

The U.S. EPA has established a Reference Concentration (RfC) of 1 milligram per cubic meter for ethyl benzene based on developmental toxicity in rats and rabbits. The U.S. EPA estimates that inhalation of this concentration or less, over a lifetime, would not likely result in the occurrence of chronic, non-cancer effects. The U.S. EPA has established an oral Reference Dose (RfD) of 0.1 milligrams per kilogram per day for ethyl benzene based on liver and kidney toxicity in rats. The U.S. EPA estimates that consumption of this dose or less, over a lifetime, will not result in the occurrence of chronic, non-cancer effects (U.S. EPA, 1994a).

No adverse human reproductive information is available. Adverse effects in fetal development have been reported in animal inhalation studies (U.S. EPA, 1994a).

Cancer: Limited and inconclusive data are available regarding the carcinogenic effects of ethyl benzene in humans and animals. The U.S. EPA has classified ethyl benzene as Group D: Not classifiable as to human carcinogenicity (U.S. EPA, 1994a). The International Agency for Research on Cancer has not classified ethyl benzene as to its carcinogenicity (IARC, 1987a).

EPA United States Environmental Protection Agency
Office of Air Quality Planning & Standards OAQPS
TTNWeb Technology Transfer Network
UATW Unified Air Toxics Website

ETHYLBENZENE

100-41-4

Hazard Summary

CAUTION: Unless otherwise noted, the quantitative information on these fact sheets are from "EPA Health Effects Notebook for Hazardous Air Pollutants-Draft", EPA-452/D-95-00, PB95-503579, December 1994." Please conduct a current literature search and check the appropriate current online database for the most recent quantitative information.

- Acute (short-term) exposure to ethylbenzene in humans results in **respiratory effects, such as throat irritation and chest constriction, irritation of the eyes, and neurological effects such as dizziness.**
- Chronic (long-term) exposure to ethylbenzene by inhalation in humans may result in effects on the blood. Animal studies have reported effects on the blood, liver, and kidneys from chronic inhalation exposure to ethylbenzene.
- The Reference Concentration (RfC) for ethylbenzene is 1 mg/m^3.[a] The U.S. Environmental Protection Agency (EPA) estimates that inhalation of this concentration or less, over a lifetime, would not likely result in the occurrence of chronic, noncancer effects.[b]
- The Reference Dose (RfD) for ethylbenzene is 0.1 mg/kg/d.[c] EPA estimates that consumption of this dose or less, over a lifetime, would not result in the occurrence of chronic, noncancer effects.
- No information is available on the developmental or reproductive effects of ethylbenzene in humans, while animal studies have reported developmental effects, including **birth defects in animals** exposed via inhalation.
- Limited information is available on the carcinogenic effects of ethylbenzene in humans or animals. EPA has classified ethylbenzene as a Group D, **not classifiable as to human carcinogenicity**.

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[a] Milligrams per cubic meter is the unit of measurement for chemicals in air.

[b] The RfC is not a direct estimator of risk but rather a reference point to gauge the potential effects. Exceedance of the RfC does not imply that an adverse health effect would necessarily occur. As the amount and frequency of exposures exceeding the RfC increase, the probability of adverse health effects also increases.

[c] Milligrams per kilogram per day is one way to measure the amount of the contaminant that is consumed

in food.

Please Note: The main sources of information for this fact sheet are EPA's Integrated Risk Information System (IRIS), which contains information on inhalation chronic toxicity of ethylbenzene and the RfC, and oral chronic toxicity and the RfD, and the Agency for Toxic Substances and Disease Registry's (ATSDR's) *Toxicological Profile for Ethylbenzene*. Other secondary sources include the Hazardous Substances Data Bank (HSDB), a database of summaries of peer-reviewed literature, and the Registry of Toxic Effects of Chemical Substances (RTECS), a database of toxic effects that are not peer reviewed.

Environmental/Occupational Exposure

- Ethylbenzene has been detected in urban air at an average concentration of 0.66 ppb. The average level in suburban air is about 0.62 ppb, while the average level measured in air in the country is about 0.01 ppb. (1)
- Indoor air usually has a higher average concentration of ethylbenzene (about 1 ppb) than ambient air, due to the use of household products such as cleaning products or paints. (1)
- Occupational exposure to ethylbenzene occurs in factories that use ethylbenzene to produce other chemicals; for gas and oil workers; and for varnish workers, spray painters, and persons involved in gluing operations. (1)
- Exposure to ethylbenzene occurs from the use of consumer products, gasoline, pesticides, solvents, carpet glues, varnishes, paints, and tobacco smoke. (1)

Assessing Personal Exposure

- Laboratory tests can determine ethylbenzene by measuring the breakdown products in the urine. (1)

Health Hazard Information

Acute Effects:

- Respiratory effects, such as throat irritation and chest constriction, irritation of the eyes, and neurological effects such as dizziness, have been noted from acute (short-term) inhalation exposure to ethylbenzene in humans. (1-3)
- Animal studies have reported central nervous system (CNS) toxicity; pulmonary effects; and effects on the liver, kidney, and eyes (irritation) from acute inhalation exposure to ethylbenzene. (1)
- Tests involving acute exposure of animals, such as the LC_{50} and LD_{50} tests in rats, have shown ethylbenzene to have moderate toxicity from inhalation and oral exposure. (1,4)

***Chronic Effects (Noncancer)*:**

- Chronic (long-term) exposure to ethylbenzene by inhalation in humans may result in effects on the blood. In a 20-year study of humans occupationally exposed to ethylbenzene, no liver toxicity was noted. (1)
- Animal studies have reported effects on the blood, liver, and kidneys from chronic inhalation exposure to ethylbenzene. (1,3)

- The RfC for ethylbenzene is 1 mg/m^3 based on developmental toxicity in rats and rabbits. (5)
- EPA has low confidence in the study on which the RfC was based because higher exposure levels may have provided more information on the potential for maternal toxicity and developmental effects; low confidence in the database because, although other studies have examined a variety of other endpoints (e.g., liver and lung), by histopathology in rats and mice, there are no chronic studies and no multigeneration developmental studies; and, consequently, low confidence in the RfC. (5)
- The RfD for ethylbenzene is 0.1 mg/kg/d based on liver and kidney toxicity in rats. (5)
- EPA has low confidence in the study on which the RfD was based because rats of only one sex were tested and the experiment was not of chronic duration; low confidence in the supporting database because other oral toxicity data were not found; and, consequently, low confidence in the RfD. (5)
- EPA's Office of Air Quality Planning and Standards, for a hazard ranking under Section 112(g) of the Clean Air Act Amendments, has evaluated ethylbenzene for chronic toxicity. Ethylbenzene has been assigned an interim composite score of 9 (scores range from 1 to 100, with 100 being the most toxic). These scores are based on a combination of values assigned to the minimal lowest-observed-adverse-effect level (LOAEL) and a ranking of the severity of the toxic effects. (6)

Reproductive/Developmental Effects:

- No information is available on the developmental or reproductive effects of ethylbenzene in humans. (1)
- Animal studies have reported developmental effects, such as fetal resorptions, retardation of skeletal development, and an increased incidence of extra ribs in animals exposed to ethylbenzene via inhalation. Mild maternal toxicity has also been reported. (1,3)

Cancer Risk:

- The only available human cancer study monitored the conditions of workers exposed to ethylbenzene for 10 years, with no tumors reported. However, no firm conclusions can be made from this study because exposure information was not provided, and 10 years is insufficient for detecting long latency tumors in humans. (1)
- A study in rats reported a statistically significant increase in malignant tumors (type unspecified) from oral exposure. However, this study is limited because no data on specific tumor type were presented and only one dose was tested. (1)
- EPA has classified ethylbenzene as a Group D, not classifiable as to human carcinogenicity. (5)

Physical Properties

- Ethylbenzene is a colorless liquid that smells like gasoline. (1)
- The odor threshold for ethylbenzene is 2.3 ppm. (7)
- The chemical formula for ethylbenzene is C_8H_{10}, and the molecular weight is 106.16 g/mol. (1)
- The vapor pressure for ethylbenzene is 9.53 mm Hg at 25 C, and its octanol/water partition coefficient (Log K_{ow}) is 3.13. (1)

Uses

- Ethylbenzene is used primarily in the production of styrene. It is also used as a solvent, as a constituent of asphalt and naphtha, and in fuels. (1)

Conversion Factors:
To convert from ppm to mg/m^3: mg/m^3 = (ppm) × (molecular weight of the compound)/(24.45). For ethylbenzene: 1 ppm = 4.34 mg/m^3.

Health Data from Inhalation Exposure

Concentration (mg/m^3)	Health numbers[a]	Regulatory, advisory numbers[b]	Reference
1,000,000.0			
-- -- -- -- 100,000.0			
-- -- -- -- 10,000.0	• LC_{50} (rats) (17,360 mg/m^3)		4
-- -- -- -- 1,000.0		• NIOSH IDLH (8,680 mg/m^3)	1,2
-- -- -- -- 100.0	• NOAEL[c] (rats and rabbits) (434 mg/m^3)	• OSHA STEL, ACGIH STEL (545 mg/m^3) • OSHA PEL, ACGIH TLV (435 mg/m^3) •	5 1,2 1,2
-- -- -- -- 10.0			

-- -- -- -- 1.0	• RfC (1 mg/m^3)		5

ACGIH STEL--American Conference of Governmental and Industrial Hygienists' short-term exposure limit; 15-min time-weighted-average exposure that should not be exceeded at any time during a workday even if the 8-h time-weighted-average is within the threshold limit value.
ACGIH TLV--American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.
LC_{50} (Lethal $Concentration_{50}$)--A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.
NIOSH IDLH--National Institute of Occupational Safety and Health immediately dangerous to life and health; NIOSH concentration representing the maximum level of a pollutant from which an individual could escape within 30 minutes without escape-impairing symptoms or irreversible health effects.
NOAEL--No-observed-adverse-effect level.
OSHA PEL--Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.
(continued)
OSHA STEL--Occupational Safety and Health Administration's short-term exposure limit; 15-min time-weighted-average exposure that should not be exceeded at any time during a workday even if the 8-h time-weighted-average is within the threshold limit value.
RfC--Reference concentration.

[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.
[c] NOAEL is from the critical study used as the basis for the EPA RfC.

References

1. Agency for Toxic Substances and Disease Registry (ATSDR). *Toxicological Profile for Ethylbenzene* (Draft). U.S. Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA. 1989.
2. E.J. Calabrese and E.M. Kenyon. *Air Toxics and Risk Assessment*. Lewis Publishers, Chelsea, MI. 1991.
3. U.S. Department of Health and Human Services. Hazardous Substances Data Bank (HSDB, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.
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(RTECS, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

5. U.S. Environmental Protection Agency. *Integrated Risk Information System (IRIS) on Ethylbenzene*. Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development, Cincinnati, OH. 1993.
6. U.S. Environmental Protection Agency. *Technical Background Document to Support Rulemaking Pursuant to the Clean Air Act--Section 112(g). Ranking of Pollutants with Respect to Hazard to Human Health*. EPA-450/3-92-010. Emissions Standards Division, Office of Air Quality Planning and Standards, Research Triangle Park, NC. 1994.
7. J.E. Amoore and E. Hautala. Odor as an aid to chemical safety: Odor thresholds compared with threshold limit values and volatilities for 214 industrial chemicals in air and water dilution. *Journal of Applied Toxicology*, 3(6):272-290. 1983.

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Ethylbenzene

CASRN 100-41-4

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0051
Ethylbenzene; CASRN 100-41-4

Health assessment information on a chemical substance is included in IRIS only after a comprehensive review of chronic toxicity data by U.S. EPA health scientists from several Program Offices and the Office of Research and Development. The summaries presented in Sections I and II represent a consensus reached in the review process. Background information and explanations of the methods used to derive the values given in IRIS are provided in the Background Documents.

STATUS OF DATA FOR Ethylbenzene

File On-Line 01/31/1987

Category (section)	Status	Last Revised
Oral RfD Assessment (I.A.)	on-line	06/01/1991
Inhalation RfC Assessment (I.B.)	on-line	03/01/1991

Carcinogenicity Assessment (II.) on-line 08/01/1991

_I. CHRONIC HEALTH HAZARD ASSESSMENTS FOR NONCARCINOGENIC EFFECTS

__I.A. REFERENCE DOSE FOR CHRONIC ORAL EXPOSURE (RfD)

Substance Name -- Ethylbenzene
CASRN -- 100-41-4
Last Revised -- 06/01/1991

The oral Reference Dose (RfD) is based on the assumption that thresholds exist for certain toxic effects such as cellular necrosis. It is expressed in units of mg/kg-day. In general, the RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. Please refer to the Background Document for an elaboration of these concepts. RfDs can also be derived for the noncarcinogenic health effects of substances that are also carcinogens. Therefore, it is essential to refer to other sources of information concerning the carcinogenicity of this substance. If the U.S. EPA has evaluated this substance for potential human carcinogenicity, a summary of that evaluation will be contained in Section II of this file.

___I.A.1. ORAL RfD SUMMARY

Critical Effect	Experimental Doses*	UF	MF	RfD
Liver and kidney toxicity	NOEL: 136 mg/kg/day (converted to 97.1 mg/kg/day)	1000	1	1E-1 mg/kg/day
Rat Subchronic to Chronic Oral Bioassay Wolf et al., 1956	LOAEL: 408 mg/kg/day (converted to 291 mg/kg/day)			

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*Conversion Factors: 5 days/7 days; thus, 136 mg/kg/day x 5 days/7 days = 97.1 mg/kg/day

I.A.2. PRINCIPAL AND SUPPORTING STUDIES (ORAL RfD)

Wolf, M.A., V.K. Rowe, D.D. McCollister, R.L. Hollingsworth and F. Oyen. 1956. Toxicological studies of certain alkylated benzenes and benzene. Arch. Ind. Health. 14: 387-398.

The chosen study is a rat 182-day oral bioassay in which ethylbenzene was given 5 days/week at doses of 13.6, 136, 408, or 680 mg/kg/day in olive oil gavage. There were 10 albino female rats/dose group and 20 controls.

The criteria considered in judging the toxic effects on the test animals were growth, mortality, appearance and behavior, hematologic findings, terminal concentration of urea nitrogen in the blood, final average organ and body weights, histopathologic findings, and bone marrow counts. The LOAEL of 408 mg/kg/day is associated with histopathologic changes in liver and kidney.

I.A.3. UNCERTAINTY AND MODIFYING FACTORS (ORAL RfD)

UF -- The uncertainty factor of 1000 reflects 10 for both intraspecies and interspecies variability to the toxicity of this chemical in lieu of specific data, and 10 for extrapolation of a subchronic effect level to its chronic equivalent.

MF --None

I.A.4. ADDITIONAL COMMENTS (ORAL RfD)

None.

I.A.5. CONFIDENCE IN THE ORAL RfD

Study -- Low
Data Base -- Low
RfD -- Low

Confidence in the chosen study is low because rats of only one sex were tested

and the experiment was not of chronic duration. Confidence in the supporting data base is low because other oral toxicity data were not found. Low confidence in the RfD follows.

___I.A.6. EPA DOCUMENTATION AND REVIEW OF THE ORAL RfD

U.S. EPA. 1980. Ambient Water Quality Criteria for Ethylbenzene. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Water Regulations and Standards, Washington, DC. EPA 440/5-80-048. NTIS PB 81-117590.

U.S. EPA. 1985. Drinking Water Criteria Document for Ethylbenzene. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Drinking Water, Washington, DC. (Public review draft)

U.S. EPA. 1985. Health Effects Assessment for Ethylbenzene. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Emergency and Remedial Response, Washington, DC. ECAO-CIN-H008.

The 1980 Ambient Water Quality Criteria Document for Ethylbenzene received extensive Agency and public review.

The 1985 Drinking Water Criteria Document for Ethylbenzene and the 1985 Health Effects Assessment for Ethylbenzene received extensive Agency review with the help of selected outside scientists.

Agency Work Group Review -- 05/20/1985

Verification Date -- 05/20/1985

___I.A.7. EPA CONTACTS (ORAL RfD)

Please contact the Risk Information Hotline for all questions concerning this assessment or IRIS, in general, at (513)569-7254 (phone), (513)569-7159 (FAX) or RIH.IRIS@EPAMAIL.EPA.GOV (internet address).

__I.B. REFERENCE CONCENTRATION FOR CHRONIC INHALATION EXPOSURE

(RfC)

Substance Name -- Ethylbenzene
CASRN -- 100-41-4
Last Revised -- 03/01/1991

The inhalation Reference Concentration (RfC) is analogous to the oral RfD and is likewise based on the assumption that thresholds exist for certain toxic effects such as cellular necrosis. The inhalation RfC considers toxic effects for both the respiratory system (portal-of-entry) and for effects peripheral to the respiratory system (extrarespiratory effects). It is expressed in units of mg/cu.m. In general, the RfC is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily inhalation exposure of the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. Inhalation RfCs were derived according to the Interim Methods for Development of Inhalation Reference Doses (EPA/600/8-88/066F August 1989) and subsequently, according to Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry (EPA/600/8-90/066F October 1994). RfCs can also be derived for the noncarcinogenic health effects of substances that are carcinogens. Therefore, it is essential to refer to other sources of information concerning the carcinogenicity of this substance. If the U.S. EPA has evaluated this substance for potential human carcinogenicity, a summary of that evaluation will be contained in Section II of this file.

___I.B.1. INHALATION RfC SUMMARY

Critical Effect	Exposures*	UF	MF	RfC
Developmental toxicity Rat and Rabbit Developmental Inhalation Studies Andrew et al., 1981; Hardin et al., 1981	NOAEL: 434 mg/cu.m (100 ppm) NOAEL(ADJ): 434 mg/cu.m NOAEL(HEC): 434 mg/cu.m LOAEL: 4340 mg/cu.m (1000 ppm) LOAEL(ADJ): 4340 mg/cu.m LOAEL(HEC): 4340 mg/cu.m	300	1	1E+0 mg/cu.m

*Conversion Factors: MW = 106.18. Assuming 25C and 760 mmHg, NOAEL(mg/cu.m) = 100 ppm x MW/24.45 = 434 mg/cu.m. For developmental effects, this concentration is not adjusted; therefore, NOAEL(ADJ) = NOAEL. The NOAEL(HEC) was calculated for a gas:extrarespiratory effect, assuming periodicity was attained. Since b:a lambda values are unknown for the experimental animal species (a) and humans (h), a default value of 1.0 was used for this ratio. NOAEL(HEC) = NOAEL(ADJ) x (b:a lambda(a)/lambda(h)) = 434 mg/cu.m.

I.B.2. PRINCIPAL AND SUPPORTING STUDIES (INHALATION RfC)

Andrew, F.D., R.L. Buschbom, W.C. Cannon, R.A. Miller, L.F. Montgomery, D.W. Phelps, et al. 1981. Teratologic assessment of ethylbenzene and 2-ethoxyethanol. Battelle Pacific Northwest Laboratory, Richland, WA. PB 83-208074., 108.

Hardin, B.D., G.P. Bond, M.R. Sikov, F.D. Andrew, R.P. Beliles and R.W. Niemeier. 1981. Testing of selected workplace chemicals for teratogenic potential. Scand. J. Work Environ. Health. 7(suppl 4): 66-75.

Inhalation experiments were conducted with Wistar rats (n=78-107/concentration) and New Zealand white rabbits (n=29-30/concentration) exposed 6 to 7 hours/day, 7 days/week during days 1-19 and 1-24 of gestation, respectively, to nominal concentrations of 0, 100, or 1000 ppm (434 or 4342 mg/cu.m) (Andrew et al., 1981). A separate group of rats was exposed pregestationally for 3 weeks prior to mating and exposure was continued into the gestational period. Actual concentrations were within 10% of target concentrations. All pregnant animals were sacrificed 1 day prior to term (21 days for rats; 30 days for rabbits). Maternal organs (liver, lungs, kidney, heart, spleen, adrenals, ovaries, and brain) were examined histopathologically. Uteri were examined and fetuses were weighed, sexed, and measured for crown-to-rump length, and examined for external, internal and skeletal abnormalities. For statistical analyses, the litter was chosen as the experimental unit.

Ethylbenzene did not elicit embryotoxicity, fetotoxicity, or teratogenicity in rabbits at either exposure level. There were no significant incidences of major malformations, minor anomalies, or common variants in fetal rabbits from exposed groups. Maternal toxicity in the rabbits was not evident. There was no evidence of histologic damage in any of the dams' organs. The principal observation noted by the investigators was a reduced number of live rabbit kits per litter ($p<0.05$) at both exposure levels when evaluated by ANOVA and Duncan's Multiple Range Test. The number of live kits per litter in the air-exposed controls was reported as 8 (3+/-s.d.), compared with 7 (3+/-s.d.) for each exposure group. However, if one recalculates the data presented in Table 9 of Andrew et al. (1981), the number of live kits per litter for the low concentration (100 ppm) was 8 rather than 7 as presented in the paper. Since the number of live kits per litter at the high concentration was 7, this may suggest an effect at 1000 ppm, but not at 100 ppm. However, the number of implantations per litter and the number of dead or resorbed per litter were not different from controls. Prenatal mortality ranged from 5 to 8% and preimplantation loss ranged from 18 to 27%. Neither indicated a concentration-related intrauterine mortality. The results of the rabbit study are indicative of a NOAEL of 100 ppm based on a lack of developmental effects in rabbits. The NOAEL(HEC) is 434 mg/cu.m.

In rats exposed only during gestation, there were no histopathological effects in any of the maternal organs examined. There was no effect on fertility or on any of the other measures of reproductive status. The principal observation in fetuses was an increased incidence ($p<0.05$) of supernumerary and rudimentary ribs in the high exposure group and an elevated incidence of extra ribs in both the high and 100 ppm groups. Both absolute and relative liver, kidney, and spleen weights were significantly increased in

pregnant rats from the 1000 ppm group.

Groups of female rats were also exposed for 3 weeks prior to mating and exposure was continued during gestation. Like the 1000-ppm group exposed only during gestation, there was also an increased incidence of extra ribs ($p<0.05$) in the pre-gestationally exposed high exposure group. However, an increased incidence was not seen at 100 ppm in those exposed pre-gestationally, in contrast to the comparable group exposed only during gestation. There was no increase in rudimentary ribs in either of exposed groups. When extra and rudimentary ribs were grouped together, there was no significant increase in supernumerary ribs in either of the exposed groups. The apparent discrepancy in the incidence of supernumerary ribs between the pregestationally-exposed group and those exposed only during gestation may be based, in part, on the fewer numbers of litters examined in the pregestationally-exposed group. There were no effects on fertility or on any of the of the other measures of reproductive status. No fetal toxicity was noted at either exposure level. Body weights, placental weights, and sex ratios were within normal limits. Absolute and relative liver and spleen weights were significantly increased in pregant rats from the 1000 ppm group; only relative kidney weight was increased significantly. There were no histopathological effects in any of the organs examined.

Skeletal variants were seen at both 434 and 4342 mg/cu.m in the rats with the effects at 432 mg/cu.m being reduced compared with those occurring at 4342 mg/cu.m. By themselves, the effects are marginally adverse, even at 4342 mg/cu.m. However, a weight-of-evidence approach, noting a cluster of other mild effects at 4342 mg/cu.m, is used to determine that 1000 ppm is a LOAEL. The skeletal variations are considered along with evidence of slightly reduced litter size in rabbits at 4342 mg/cu.m and an increase in "% skeletal retarded fetuses" at 600 mg/cu.m (Ungvary and Tatrai, 1985). Additional support for this position is derived from the observations of somewhat elevated maternal liver, kidney, and spleen weights (Andrew et al., 1981).

___I.B.3. UNCERTAINTY AND MODIFYING FACTORS (INHALATION RfC)

UF -- The uncertainty factor of 300 reflects a factor of 10 to protect unusually sensitive individuals, 3 to adjust for interspecies conversion and 10 to adjust for the absence of multigenerational reproductive and chronic studies.

MF -- None

___I.B.4. ADDITIONAL STUDIES / COMMENTS (INHALATION RfC)

Ungvary and Tatrai (1985) exposed CFY rats (n=17-20) to levels of 600, 1200, or 2400 mg/cu.m for 24 hours/day during days 7 to 15 of gestation. CFLP

mice (n=20) were exposed to 500 mg/cu.m for 24 hours/day from gestational days 6 to 15 or for 3 days intermittently for 4 hours/day for days 6-15. It is not clear from the description if the results pertain to the continuous exposure or the intermittent exposure. New Zealand rabbits (n=3-9) were exposed for 24 hours/day to concentrations of 500 or 1000 mg/cu.m from gestational days 7 to 20. Untreated animals and those exposed to air only served as controls.

It was stated that maternal toxicity (unspecified species) was moderate and concentration-dependent; however, no data were presented to support this statement. Maternal weight gain was reported to have decreased for rabbits exposed to 1000 mg/cu.m. It was reported that rabbits exposed to 1000 mg/cu.m exhibited mild maternal toxicity manifested by reduced weight gain. However, the percent weight gain was not reported. There were no data for developmental endpoints in the 1000-ppm group because there were no live fetuses. One dam had died and three others aborted in this exposure group. Four dams had total resorptions. However, four other compounds in addition to ethyl benzene were tested at 1000 mg/cu.m and all caused spontaneous abortions at this level. Thus, the results are not clearly indicative of a treatment-related effect. This observation, coupled with the lack of any indication of abortions in rabbits in the Hardin et al. (1981) study, suggests that this effect in rabbits is not treatment-related.

Ungvary and Tatrai (1985) did observe a significant reduction in the mean female fetal weight in rabbit dams exposed 24 hours/day to 500 mg/cu.m. Andrew et al. (1981) did not observe such an effect in rabbits exposed up to 4348 mg/cu.m. These conflicting results in rabbits might be attributable to differences in study design.

Postimplantation loss (% dead or resorbed fetuses), and exposure-related skeletal retardation were significantly elevated ($p<0.05$) in rats at all exposure levels with one exception. Exposure to 600 mg/cu.m for 6 hours/day (it was not stated if this was a single exposure or the exposure duration on each day of gestation) did not result in any statistically significant fetal effects although there was increased incidence of dead/resorbed fetuses, lower weight of fetuses, and skeletal retarded fetuses. In the 24-hour/day exposure groups, malformations characterized as "anomalies of the uropoietic apparatus" and an increased incidence of extra ribs were significantly increased only at the highest exposure level. No data were presented on the anomalies of the uropoeitic apparatus. There was a significant ($p<0.05$) increase in skeletal retardation and fetal resorption in all continuous exposure groups although the concentration-response was shallow. The percent skeletal retarded fetuses, for example, at exposure concentrations of 600, 1200, and 2400 mg/cu.m was 26, 30, and 35%, respectively; the incidence in controls was 13%. These results in rats suggest a LOAEL(HEC) of 2400 mg/cu.m for extra ribs in the absence of demonstrable maternal toxicity.

In mice, an increased incidence of "anomalies of the uropoietic apparatus" was the only observation, but no data were presented. There was no discussion concerning maternal toxicity.

A 90-day subchronic inhalation study was conducted in F344/N rats (n=10/sex/group) and B6C3F1 mice (n=10/sex/group) that were exposed to 0, 100, 250, 500, 750, and 1000 ppm (0, 434, 1086, 2171, 3257, and 4343 mg/cu.m) 6 hours/day, 5 days/week (NTP, 1988; 1989; 1990). The duration-adjusted values were 0, 77.5, 194, 388, 582, and 776 mg/cu.m, respectively. The test

atmosphere concentrations monitored by gas chromatography were within a 10% range of the target concentrations. At study termination, necropsies were conducted on the lung, liver, kideny, heart, testes, and thymus with organ weight measurements. Clinical chemistry data were obtained for rats. Histopathological examinations were conducted on all animals in the high concentration groups and in controls; animals in the lower concentration groups were evaluated when lesions were observed until no observed effects were seen. Sperm morphology and vaginal cytology tests were performed. There were no mortalities, exposure-related clinical signs of toxicity, or significant adverse effects on body weight in any of the exposed rats or mice.

In rats, hematology parameters were unaffected. Of the liver enzymes evaluated, only serum alkaline phosphatase (SAP) activity was significantly reduced in a concentration-related manner (at 500 ppm and above) for both sexes with a greater sensitivity in females. The significance of this decrease is not clear since in liver damage, SAP levels usually increase. The investigators suggested the decrease may be due to reduced water and food intake. No liver histopathology was noted for any exposure group. Significant concentration-related increases in absolute liver weights occurred in males at 250 ppm and higher (12.5, 17.3, 22.0, and 23.6% at 250, 500, 750, and 1000 ppm, respectively); in females the lowest concentration at which an increase in absolute liver weight was seen was in the 500-ppm group (11.8%). The increase in the 750- and 1000-ppm groups was 11.5 and 15.8%, respectively. Relative liver weights were significantly increased in all male exposure groups except the 100-ppm group while all female exposure groups except the two lowest groups showed significant increases. Absolute kidney weight in males significantly increased only in the 500- and 750-ppm groups; relative weight was increased in the three highest exposure groups. In females, both absolute and relative kidney weights increased significantly in the three highest exposure groups. Regeneration of renal tubules in the kidneys of male rats only was seen in all groups including controls. The severity of the lesions was greatest in the rats at in the high-exposure group.

The most significant gross observation in rats was the presence of enlarged bronchial and/or mediastinal lymph nodes, but these observations were not dose-related. The incidence for minimal lung inflammation in male rats was 0/10, 3/10, 9/10, 9/10, 8/10, and 10/10 for the 0-, 100-, 250-, 500-, 750-, and 1000-ppm exposure groups, respectively. Microscopically, this enlargement was attributable to an increase in normal constituents of the lymph nodes characterized by accumulations of macrophages, lymphocytes, neutrophils, and plasma cells. It was the opinion of the NTP Pathology Working Group (PWG) that hyperplasia of the lymph nodes and lower respiratory tract was typical of an infectious agent with an associated active immune response rather than ethylbenzene exposure (NTP, 1989). This diagnosis was supported by the following observations: an uneven distribution of lesions among and within groups; foci of airway inflammation were randomly distributed throughout the lungs; considerable variability in severity within groups; and there was no consistent concentration-response relationship. No lesions were seen in the nasal cavity. The PWG described these lesions as not typical of the type of lesions which occurs with known pulmonary irritants. These lesions were not found in control animals, which were housed in separate rooms. No infectious agent was identified upon serologic examination. In the draft NTP technical report (NTP, 1990), the inflammatory lung lesions were described as probably unrelated to exposure. Antibodies to common rodent respiratory tract viruses were not detected. However, only sera from control

rats were sampled. Lesions morphologically indistinguishable from those in this study have been seen in control and treatment groups of rats from other inhalation and dosed feed studies (NTP, 1990). The PWG recommended that this effect be reevaluated in another study.

In mice, no significant exposure-related gross or histopathological observations were noted at terminal necropsy of any organs, including the lung. The only exposure-related effects were significantly elevated absolute and relative liver weight in both sexes of mice at of 750 and 1000 ppm and significantly elevated relative kidney weight of the females exposed to 1000 ppm. There were no significant histopathological changes or function test alterations in either liver or kidney of either sex.

The NTP peer review of the subchronic study took place on November 20, 1990 at Research Triangle Park. The NTP Board of Scientific Counselors' panel of experts agreed with the conclusions of the NTP report that there were no indications of toxicity due to ethyl benzene. A 2-year lifetime study in both rats and mice has been initiated and exposures have been conducted through 7 months. No serial sacrifices are planned and results are not expected prior to 1992.

Clark (1983) exposed Wistar rats (n=18/sex/group) (12-13 weeks old) to 0 and 100 ppm (0 and 434 mg/cu.m) reagent grade ethylbenzene 6 hours/day, 5 days/week for 12 weeks. The duration-adjusted values were 0 and 77.5 mg/cu.m. Clinical observations, body weight, food intake, hematology, urinalysis, organ weights, and histopathology of all major organs (including the lung and nasal cavity) were used as parameters to assess toxicity. No statistically significant effects were observed at 100 ppm. There were no differences from controls in the liver enzymes, including SAP. While slight bile duct hyperplasia was seen in 15/18 exposed males and 14/18 exposed females, hyperplasia was also common in controls (10/18 females and 8/18 males), and these observations were not statistically significant. The results of this study suggest a NOAEL of 100 ppm. The NOAEL(HEC) is 77.5 mg/cu.m. The results are in general agreement with the findings of the NTP study in F344 rats.

Wolf et al. (1956) exposed rats (n=10-25/sex/group) to 400, 600 or 1250 ppm (1737, 2606, or 5428 mg/cu.m) ethylbenzene 7 hours/day, 5 days/week for about 6 months. The duration-adjusted values were 0, 362, 542, and 1131 mg/cu.m, respectively, using the 7-hour duration. Exposure ranged from 186 to 214 days. Male rats only were also exposed to 2200 ppm (9554 mg/cu.m) for 7 hours/day, 5 days/week for about 5 months. The duration-adjusted value was 1990 mg/cu.m. Histopathology was performed on a variety of organs including the lung. Data on liver and kidney weights and histopathology were not presented; these parameters were discussed only in descriptive terms. Repeated exposure of rats, guinea pigs, and rhesus monkeys was examined.

Growth was depressed moderately in male rats at 2200 ppm. Liver and kidney weights in rats were increased slightly in all exposed groups compared with matched controls, and rats exposed to 1250 and 2200 ppm developed histopathological changes manifested as cloudy swelling of the liver and renal tubules and testicular degeneration. The date indicate a NOAEL for liver histopatholgy at 600 ppm (542 mg/cu.m). However, no incidence data was reported. Since it is not clear that these effects are adverse when taken in context with the results of the NTP study, a NOAEL or LOAEL is not identified.

Guinea pigs (5-10/sex/group) and rabbits (1-2/sex/group) were exposed to 0, 400, or 600 ppm (duration-adjusted concentrations of 0, 362, or 542 mg/cu.m, respectively) ethylbenzene 7 hours/day, 5 days/week for about 6 months. Only females were exposed to 1250 ppm (duration-adjusted value of 1131 mg/cu.m). Growth was depressed in female guinea pigs exposed to 1250 ppm. Liver weight was described as slightly increased only in the 600-ppm exposure group. The study does not clearly indicate 600 ppm as a LOAEL so the NOAEL for guinea pigs is designated at 600 ppm. The NOAEL(HEC) is 542 mg/cu.m. Other than an observation of slight degeneration of the testicular germinal epithelium in the male rabbit at 600 ppm, there were no adverse effects reported for rabbits of either sex.

One male Rhesus monkey was exposed to 600 ppm (duration-adjusted value of 542 mg/cu.m) and two females were exposed to 400 ppm (duration-adjusted value of 362 mg/cu.m). A slight degeneration of the testicular germinal epithelium and increased liver weight was observed in the male monkey. No effects were reported for the female rhesus monkeys.

The small number of rabbits and monkeys preclude identification of NOAEL and LOAEL values for these species.

Cragg et al. (1989) exposed B6C3F1 mice (n=5/sex/group) and F344 rats (n=5/sex/group) to actual concentrations of 0, 99, 382, and 782 ppm (0, 430, 1659, and 3396 mg/cu.m) 6 hours/day, 5 days/week for 4 weeks. The duration-adjusted values were 0, 77, 296, 606 mg/cu.m, respectively. In the same study, New Zealand White rabbits (n=5/sex/group) were exposed to actual concentrations of 0, 382, 782, or 1610 ppm (0, 1659, 3396, or 6992 mg/cu.m). The duration-adjusted values were 0, 296, 606 and 1249 mg/cu.m, respectively. No changes were evident in mortality, clinical chemistry parameters, urinalysis, nor were there treatment-related gross or histopathological findings. Urinalysis was not performed on rabbits and clinical chemistry parameters were not performed on mice. Liver enzymes measured included AP. Hematology was performed on all species. Histopathology was only conducted on the high concentration animals except all rabbits' testes were examined. There was no liver histopathology in any of the species.

In the 382-ppm exposure group, rats exhibited sporadic incidences of salivation and lacrimation. (These observations were not noted in the NTP subchronic study). Absolute liver weights were significantly increased in male rats; relative weight was increased at 782 ppm. In females, absolute liver weight was significantly increased at 782 ppm and relative weight at both concentrations. Male rats of the 782 ppm group had a significant ($p<0.05$) increase in platelets while females only had a significant ($p<0.05$) increase in total leukocytes.

In mice, females showed a statistically significant increase in absolute, but not relative liver weight, at 782 ppm. There were no significant liver weight changes in male mice. Both males and females exhibited an increased liver weight relative to brain weight at 782 ppm only. Rabbits showed no changes in liver weight ratios at any exposure level.

Since there were no adverse histopathological findings for the liver, a NOAEL of 782 ppm is identified for rats and mice. The NOAEL(HEC) is 606 mg/cu.m. The NOAEL for rabbits is 1610 ppm; the NOAEL(HEC) is 1249 mg/cu.m.

Elovaara et al. (1985) found concentration-related increases in drug-metabolizing enzymes of liver and kidney, with corresponding ultrastructural alterations in a subchronic inhalation study with rats. Male Wistar rats (n=5/group) were exposed to 0, 50, 300, or 600 ppm (0, 217, 1302, or 2604 mg/cu.m) ethylbenzene 6 hours/day, 5 days/week for 2, 5, 9, or 16 weeks. The duration-adjusted values were 0, 38.7, 233, and 465 mg/cu.m, respectively. The liver was the only organ examined histologically (light and electron microscopy). There were no changes in liver weight at any concentration. After 16 weeks exposure, NADPH-cytochrome reductase and UDPG-transferase were significantly elevated at 300 and 600 ppm. Aminopyrine N-demethylase and 7-ethoxycoumarin-0-deethylase (7-ECDE) were elevated at all exposure levels. The elevation in UDPG-transferase was exposure-related and may signify glucuronidation of ethylbenzene metabolites during detoxication. Electron microscopy also showed changes in hepatocyte ultrastructure [e.g., smooth endoplasmic reticulum (SER) proliferation, slight degranulation of rough endoplasmic reticulum] at all exposure levels beginning 2 to 9 weeks after exposure. Necrosis was not observed nor were there any increases in serum alanine aminotransferase. SAP was not measured. The proliferation of SER is consistent with enzyme induction. At 16 weeks, changes in ultrastructure were mainly confined to the high-exposure group. There was no effect of exposure on hepatic glutathione (GSH) content. Significant increases in relative kidney weight only were reported following 2 and 9, but not at 16 weeks of exposure to 600 ppm. Kidney 7-ECDE, and UDPG transferase activities showed statistically significant and exposure-related increases at all exposure levels.

In the absence of histologic evidence of damage, changes in absolute or relative liver weight, and no effect on serum ALT, the microsmal enzyme induction and ultrastructural changes are considered to be adaptation phenomena. The results of this study suggest a NOAEL of 600 ppm. The NOAEL(HEC) is 465 mg/cu.m for liver and kidney. The absence of liver weight changes is not consistent with the findings of the NTP (1988) subchronic study.

Angerer and Wulf (1985) evaluated 35 workers who chronically (2-24 years, average 8.2 years) sprayed varnishes containing alkyd-phenol and polyester resins dissolved in solvent mixtures consisting principally of xylene isomers and ethylbenzene. Some of the varnishes contained lead-based pigments. The air samples from personal monitors indicated average levels of 4.0 ppm for ethylbenzene. Although workers had significantly elevated lymphocytes in addition to significantly decreased erythrocyte counts and hemoglobin levels compared with controls, these effects cannot be attributed to ethylbenzene since other compounds (e.g., xylene, methylchloroform, n-butanol, toluene, C9 hydrocarbons) were detected in some of the six workplaces evaluated.

Bardodej and Cirek (1988) carried out biomonitoring of 200 ethylbenzene production workers occupationally exposed for a mean duration of 12.2 years to unspecified concentrations of ethylbenzene and benzene over a 20-year period. The workers were evaluated twice a year and ethylbenzene metabolites measured. No statistically significant differences in hematological effects (e.g., RBC, WBC, leukocyte and platelet counts) or liver function tests (e.g., aminotransferase and/or SAP and LDH activities and bilirubin tests) were observed between exposed and nonexposed workers.

I.B.5. CONFIDENCE IN THE INHALATION RfC

Study -- Low
Data Base -- Low
RfC -- Low

The developmental study by Hardin et al. (1981) was well-conducted and indicated no clearly adverse effects in any species. The study is given a low confidence rating because higher exposure levels may have provided more information on the potential for maternal toxicity and developmental effects. The data base is given a low rating since although other studies have examined a variety of other endpoints (e.g., liver and lung), by histopathology in rats and mice, there are no chronic studies and no multi-generation developmental studies. These latter studies would be useful to determine more conclusively the potential of ethylbenzene to affect development.

NTP does not consider observations of lung lesions in rats exposed in the NTP subchronic study to be treatment-related. However, no infectious agent has been detected. Therefore, there remains a possibility that ethylbenzene may play a role in producing lung lesions. It is anticipated that this issue will be clarified upon completion of the chronic study in progress.

In view of the previous considerations, the RfC is given a low confidence rating.

I.B.6. EPA DOCUMENTATION AND REVIEW OF THE INHALATION RfC

Source Document -- This assessment is not presented in any existing U.S. EPA document.

Other EPA Documentation -- U.S. EPA, 1984; 1985; 1987

Agency Work Group Review -- 09/19/1990, 12/20/1990

Verification Date -- 12/20/1990

I.B.7. EPA CONTACTS (INHALATION RfC)

Please contact the Risk Information Hotline for all questions concerning this assessment or IRIS, in general, at (513)569-7254 (phone), (513)569-7159 (FAX) or RIH.IRIS@EPAMAIL.EPA.GOV (internet address).

_II. CARCINOGENICITY ASSESSMENT FOR LIFETIME EXPOSURE

Substance Name -- Ethylbenzene
CASRN -- 100-41-4
Last Revised -- 08/01/1991

Section II provides information on three aspects of the carcinogenic assessment for the substance in question; the weight-of-evidence judgment of the likelihood that the substance is a human carcinogen, and quantitative estimates of risk from oral exposure and from inhalation exposure. The quantitative risk estimates are presented in three ways. The slope factor is the result of application of a low-dose extrapolation procedure and is presented as the risk per (mg/kg)/day. The unit risk is the quantitative estimate in terms of either risk per ug/L drinking water or risk per ug/cu.m air breathed. The third form in which risk is presented is a drinking water or air concentration providing cancer risks of 1 in 10,000, 1 in 100,000 or 1 in 1,000,000. The rationale and methods used to develop the carcinogenicity information in IRIS are described in The Risk Assessment Guidelines of 1986 (EPA/600/8-87/045) and in the IRIS Background Document. IRIS summaries developed since the publication of EPA's more recent Proposed Guidelines for Carcinogen Risk Assessment also utilize those Guidelines where indicated (Federal Register 61(79):17960-18011, April 23, 1996). Users are referred to Section I of this IRIS file for information on long-term toxic effects other than carcinogenicity.

__II.A. EVIDENCE FOR CLASSIFICATION AS TO HUMAN CARCINOGENICITY

___II.A.1. WEIGHT-OF-EVIDENCE CLASSIFICATION

Classification -- D; not classifiable as to human carcinogenicity.

Basis -- nonclassifiable due to lack of animal bioassays and human studies.

___II.A.2. HUMAN CARCINOGENICITY DATA

None.

II.A.3. ANIMAL CARCINOGENICITY DATA

None. NTP has plans to initiate bioassay. Metabolism and excretion studies at 3.5, 35 and 350 mg/kg are to be conducted as well.

II.A.4. SUPPORTING DATA FOR CARCINOGENICITY

The metabolic pathways for humans and rodents are different (Engstrom et al., 1984). Major metabolites in humans, mandelic acid and phenylglyoxylic acid, are minor metabolites in rats and rabbits (Kiese and Lenk, 1974). The major animal metabolites were not detected in the urine of exposed workers (Engstrom et al., 1984).

Ethylbenzene at 0.4 mg/plate was not mutagenic for Salmonella strains TA98, TA1535, TA1537 and TA1538 with or without Aroclor 1254 induced rat liver homogenates (S9) (Nestmann et al., 1980). Ethylbenzene was shown to increase the mean number of sister chromatid exchanges in human whole blood lymphocyte culture at the highest dose examined without any metabolic activation system (Norppa and Vainio, 1983).

Dean et al. (1985) used a battery of short-term tests including bacterial mutation assays, mitotic gene conversion in Saccharomyces cerevisiae JD1 in the presence and absence of S9 and chromosomal damage in a cultured rat liver cell line. Ethylbenzene was not mutagenic in the range of concentrations tested (0.2, 2, 20, 50 and 200 ug/plate) for S. typhimurium TA98, TA100, TA1535, TA1537 and TA1538 or for Escherichia coli WP2 and WP2uvrA. Ethylbenzene also showed no response in the S. cerevisiae JD1 gene conversion assay. In contrast, ethylbenzene hydroperoxide showed positive responses with E. coli WP2 at 200 ug/plate in the presence of S9 and an equally significant response with the gene conversion system of yeast.

II.B. QUANTITATIVE ESTIMATE OF CARCINOGENIC RISK FROM ORAL EXPOSURE

Not available.

__II.C. QUANTITATIVE ESTIMATE OF CARCINOGENIC RISK FROM INHALATION EXPOSURE

Not available.

__II.D. EPA DOCUMENTATION, REVIEW, AND CONTACTS (CARCINOGENICITY ASSESSMENT)

___II.D.1. EPA DOCUMENTATION

Source Document -- U.S. EPA, 1980, 1984, 1987

The Ambient Water Quality Criteria Document and the Health Assessment Document have received Agency and external review. The Drinking Water Criteria Document has been extensively reviewed.

___II.D.2. REVIEW (CARCINOGENICITY ASSESSMENT)

Agency Work Group Review -- 10/07/1987

Verification Date -- 10/07/1987

___II.D.3. U.S. EPA CONTACTS (CARCINOGENICITY ASSESSMENT)

Please contact the Risk Information Hotline for all questions concerning this assessment or IRIS, in general, at (513)569-7254 (phone), (513)569-7159 (FAX)

or RIH.IRIS@EPAMAIL.EPA.GOV (internet address).

_VI. BIBLIOGRAPHY

Substance Name -- Ethylbenzene
CASRN -- 100-41-4
Last Revised -- 03/01/1991

__VI.A. ORAL RfD REFERENCES

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VI.C. CARCINOGENICITY ASSESSMENT REFERENCES

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U.S. EPA. 1984. Health Effects Assessment for Ethylbenzene. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Emergency and Remedial Response, Washington, DC.

U.S. EPA. 1987. Drinking Water Criteria Document for Ethylbenzene. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Drinking Water, Washington, DC. (Final report)

_VII. REVISION HISTORY

Substance Name -- Ethylbenzene
CASRN -- 100-41-4

Date	Section	Description
03/01/1988	I.A.1.	Dose conversion clarified
03/01/1988	I.A.6.	Documentation revised
03/01/1988	III.A.	Health Advisory added
09/07/1988	II.	Carcinogen summary on-line
08/01/1989	VI.	Bibliography on-line
08/01/1990	IV.F.1.	EPA contact changed
10/01/1990	I.B.	Inhalation RfC now under review
03/01/1991	I.B.	Inhalation RfC summary on-line
03/01/1991	VI.B.	Inhalation RfC references added
06/01/1991	I.A.7.	Primary contact changed
08/01/1991	II.D.3.	Secondary contact changed
01/01/1992	I.A.7.	Secondary contact changed
01/01/1992	IV.	Regulatory actions updated
04/01/1997	III.,IV., V.	Drinking Water Health Advisories, EPA Regulatory Actions, and Supplementary Data were removed from IRIS on or before April 1997. IRIS users were directed to the appropriate EPA Program Offices for this information.

VIII. SYNONYMS

Substance Name -- Ethylbenzene
CASRN -- 100-41-4
Last Revised -- 01/31/1987

100-41-4
AETHYLBENZOL
BENZENE, ETHYL
EB
ETHYLBENZEEN
Ethylbenzene
ETHYLBENZOL
ETILBENZENE
ETYLOBENZEN
NCI-C56393

PHENYLETHANE
UN 1175
.

IRIS Home Page | Substance File List

Send Comments | Search | NCEA Home Page | ORD Home Page | EPA Home Page

Last updated: **5 May 1998**
URL: http://www.epa.gov/iris/subst/0051.htm

Drinking Water and Health

As part of the Drinking Water and Health pages, this fact sheet is part of a larger publication:

National Primary Drinking Water Regulations

Consumer Factsheet on: ETHYLBENZENE

This is a factsheet about a chemical that may be found in some public or private drinking water supplies. It may cause health problems if found in amounts greater than the health standard set by the United States Environmental Protection Agency (EPA).

What is Ethylbenzene and how is it used?

Ethylbenzene is a colorless organic liquid with a sweet, gasoline-like odor. The greatest use - over 99 percent - of ethylbenzene is to make styrene, another organic liquid used as a building block for many plastics. It is also used as a solvent for coatings, and in making rubber and plastic wrap.

The list of trade names given below may help you find out whether you are using this chemical at home or work.

Trade Names and Synonyms:

Ethylbenzol
Phenylethane

Why is Ethylbenzene being Regulated?

In 1974, Congress passed the Safe Drinking Water Act. This law requires EPA to determine safe levels of chemicals in drinking water which do or may cause health problems. These non-enforceable levels, based solely on possible health risks and exposure, are called Maximum Contaminant Level Goals.

The MCLG for ethylbenzene has been set at 0.7 parts per million (ppm) because EPA believes this level of protection would not cause any of the potential health problems described below.

Based on this MCLG, EPA has set an enforceable standard called a Maximum Contaminant Level (MCL). MCLs are set as close to the MCLGs as possible, considering the ability of public water systems to detect and remove contaminants using suitable treatment technologies.

The MCL has also been set at 0.7 ppm because EPA believes, given present technology and resources, this is the lowest level to which water systems can reasonably be required to remove this contaminant should it occur in drinking water.

These drinking water standards and the regulations for ensuring these standards are met, are called National Primary Drinking Water Regulations. All public water supplies must abide by these regulations.

What are the Health Effects?

Short-term: EPA has found ethylbenzene to potentially cause the following health effects when people are exposed to it at levels above the MCL for relatively short periods of time: drowsiness, fatigue, headache and mild eye and respiratory irritation.

Long-term: Ethylbenzene has the potential to cause the following effects from a lifetime exposure at levels above the MCL: damage to the liver, kidneys, central nervous system and eyes.

How much Ethylbenzene is produced and released to the environment?

Production of ethylbenzene has increased: from 6.9 billion lbs. in 1982 to 11.8 billion lbs in 1993. It is released to the air primarily from its use in gasoline. More localized may be due to waste water and spills from its production and industrial use.

From 1987 to 1993, according to EPA's Toxic Chemical Release Inventory, ethylbenzene releases to water and land totalled over 761,000 lbs. These releases were primarily from petroleum refining industries. The largest releases occurred in Texas. The largest direct releases to water occurred in Virginia.

What happens to Ethylbenzene when it is released to the environment?

Ethylbenzene will evaporate rapidly from water, and will be degraded by microbes. It binds only moderately to aquatic sediment and to soils. Thus, it may leach to ground water if released to land. Ethylbenzene has little potential for accumulating in aquatic life.

How will Ethylbenzene be Detected in and Removed from My Drinking Water?

The regulation for ethylbenzene became effective in 1992. Between 1993 and 1995, EPA required your water supplier to collect water samples every 3 months for one year and analyze them to find out if ethylbenzene is present above 0.5 ppb. If it is present above this level, the system must continue to monitor this contaminant.

If contaminant levels are found to be consistently above the MCL, your water supplier must take steps to reduce the amount of ethylbenzene so that it is consistently below that level. The following treatment methods have been approved by EPA for removing ethylbenzene: Granular activated charcoal in combination with Packed Tower Aeration.

How will I know if Ethylbenzene is in my drinking water?

If the levels of ethylbenzene exceed the MCL, 0.7 ppm, the system must notify the public via newspapers, radio, TV and other means. Additional actions, such as providing alternative drinking water supplies, may be required to prevent serious risks to public health.

Drinking Water Standards:

Mclg: 0.7 ppm

Mcl: 0.7 ppm

Ethylbenzene Releases to Water and Land, 1987 to 1993 (in pounds):

	Water	Land
TOTALS (in pounds)	**47,293**	**714,580**
Top Ten States		
TX	9,870	480,164
VI	1,233	72,245
IL	31	44,789
PR	0	23,980
VA	17,997	1,950
DE	3,460	13,324
NJ	1,892	11,510
NM	0	13,076
WY	250	12,755
LA	4,383	4,552
Major Industries		
Petroleum refining	55,201	718,884
Plastics, resins	12,384	9,212
Indust. Organics	10,683	9,781
Pharmaceuticals	14,090	0
Metal containers	0	11,510

* Water/Land totals only include facilities with releases greater than a certain amount - usually 1000 to 10,000 lbs.

Learn more about your drinking water!

EPA strongly encourages people to learn more about their drinking water, and to support local efforts to protect and upgrade the supply of safe drinking water. Your water bill or telephone books government listings are a good starting point.

Your local water supplier can give you a list of the chemicals they test for in your water, as well as how your water is treated.

Your state Department of Health/Environment is also a valuable source of information.

For help in locating these agencies or for information on drinking water in general, call: EPAs Safe Drinking Water Hotline: (800) 426-4791.

For additional information on the uses and releases of chemicals in your state, contact the: Community Right-to-Know Hotline: (800) 535-0202.

Revised *January 26, 1998*



Office of Ground Water and Drinking Water

http://www.epa.gov/OGWDW/dwh/c-voc/ethylben.html

International Chemical Safety Cards

ETHYLBENZENE

ICSC: 0268

ETHYLBENZENE
Ethylbenzol
Phenylethane
EB
$C_8H_{10}/C_6H_5-C_2H_5$
Molecular mass: 106.2

CAS # 100-41-4
RTECS # DA0700000
ICSC # 0268
UN # 1175
EC # 601-023-00-4



TYPES OF HAZARD/ EXPOSURE	ACUTE HAZARDS/ SYMPTOMS	PREVENTION	FIRST AID/ FIRE FIGHTING
FIRE	Highly flammable.	NO open flames, NO sparks, and NO smoking.	Powder, AFFF, foam, carbon dioxide.
EXPLOSION	Vapour/air mixtures are explosive.	Closed system, ventilation, explosion-proof electrical equipment and lighting. Do NOT use compressed air for filling, discharging, or handling.	In case of fire: keep drums, etc., cool by spraying with water.
EXPOSURE		PREVENT GENERATION OF MISTS!	
• **INHALATION**	Cough. Dizziness. Drowsiness. Headache.	Ventilation, local exhaust, or breathing protection.	Fresh air, rest. Refer for medical attention.
• **SKIN**	Dry skin. Redness.	Protective gloves.	Remove contaminated clothes. Rinse and then wash skin with water and soap.
• **EYES**	Redness. Pain. Blurred vision.	Face shield or eye protection in combination with breathing protection.	First rinse with plenty of water for several minutes (remove contact lenses if easily possible), then take to a doctor.

• **INGESTION**	(further see Inhalation).	Do not eat, drink, or smoke during work.	Rinse mouth. Give a slurry of activated charcoal in water to drink. Refer for medical attention.

SPILLAGE DISPOSAL	STORAGE	PACKAGING & LABELLING
Ventilation. Collect leaking liquid in covered containers. Absorb remaining liquid in sand or inert absorbent and remove to safe place. Do NOT wash away into sewer (extra personal protection: A filter respirator for organic vapour).	Fireproof. Separated from strong oxidants.	F symbol Xn symbol R: 11-20 S: (2-)16-24/25-29 UN Hazard Class: 3 UN Packing Group: II

SEE IMPORTANT INFORMATION ON BACK

ICSC: 0268

Prepared in the context of cooperation between the International Programme on Chemical Safety & the Commission of the European Communities © IPCS CEC 1993 No modifications to the International version have been made except to add the OSHA PELs, NIOSH RELs and IDLH values.

International Chemical Safety Cards

ETHYLBENZENE

ICSC: 0268

IMPORTANT DATA

PHYSICAL STATE; APPEARANCE:
COLOURLESS LIQUID , WITH AROMATIC ODOUR.

PHYSICAL DANGERS:
The vapour mixes well with air, explosive mixtures are easily formed.

CHEMICAL DANGERS:
Reacts with strong oxidants. Attacks plastic and rubber.

OCCUPATIONAL EXPOSURE LIMITS (OELs):
TLV (as TWA): 100 ppm; 434 mg/m^3; as STEL: 125 ppm; 543 mg/m^3 (ACGIH 1994-1995).
MAK: 100 ppm; 440 mg/m^3 (1994).
OSHA PEL: TWA 100 ppm (435 mg/m^3)
NIOSH REL: TWA 100 ppm (435 mg/m^3) ST 125 ppm (545 mg/m^3)
NIOSH IDLH: 800 ppm LEL

ROUTES OF EXPOSURE:
The substance can be absorbed into the body by inhalation of its vapour, through the skin and by ingestion.

INHALATION RISK:
A harmful contamination of the air will be reached rather slowly on evaporation of this substance at 20°C.

EFFECTS OF SHORT-TERM EXPOSURE:
The substance irritates the eyes, the skin and the respiratory tract. Swallowing the liquid may cause aspiration into the lungs with the risk of chemical pneumonitis. The substance may cause effects on the central nervous system. Exposure far above OEL could cause lowering of consciousness.

EFFECTS OF LONG-TERM OR REPEATED EXPOSURE:
Repeated or prolonged contact with skin may cause dermatitis.

PHYSICAL PROPERTIES	Boiling point: 136°C Melting point: -95°C Relative density (water = 1): 0.9 Solubility in water, g/100 ml at 20°C: 0.015 Vapour pressure, kPa at 20°C: 0.9 Relative vapour density (air = 1): 3.7 Relative density of the vapour/air-mixture at 20°C (air = 1): 1.02 Flash point: 18°C c.c. Auto-ignition temperature: 432°C Explosive limits, vol% in air: 1.0-6.7 Octanol/water partition coefficient as log Pow: 3.2
ENVIRONMENTAL DATA	The substance is harmful to aquatic organisms. 

N O T E S

The odour warning when the exposure limit value is exceeded is insufficient.

Transport Emergency Card: TEC (R)-522
NFPA Code: H2; F3; R0

ADDITIONAL INFORMATION

ICSC: 0268 **ETHYLBENZENE**

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IMPORTANT LEGAL NOTICE:	Neither NIOSH, the CEC or the IPCS nor any person acting on behalf of NIOSH, the CEC or the IPCS is responsible for the use which might be made of this information. This card contains the collective views of the IPCS Peer Review Committee and may not reflect in all cases all the detailed requirements included in national legislation on the subject. The user should verify compliance of the cards with the relevant legislation in the country of use. The only modifications made to produce the U.S. version is inclusion of the OSHA PELs, NIOSH RELs and IDLH values.

Level 1

Chemical Name: Ethylbenzene

CAS Registry Number: 100-41-4

Click on red circle(s) to obtain data.

Risk Value	ATSDR	Health Canada	ITER	RIVM	U.S.EPA	WHO/IPCS
Noncancer Oral	●	●	●	●	●	●
Cancer Oral	●	●	●	●	●	●
Noncancer Inhalation	●	●	●	●	●	●
Cancer Inhalation	●	●	●	●	●	●

Glossary of ITER definitions

ITER Instructions

WHAT'S NEW | SUPPORT ITER | ITER HOME | RETURN

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CTC Concurrent Technologies Corporation

Toxicology Excellence for Risk Assessment

TERA

NTP CHEMICAL REPOSITORY (RADIAN CORPORATION, AUGUST 29, 1991)
ETHYLBENZENE

-IDENTIFIERS
 ===========

*CATALOG ID NUMBER: 000486

*CAS NUMBER: 100-41-4

*BASE CHEMICAL NAME: ETHYLBENZENE

*PRIMARY NAME: ETHYLBENZENE

*CHEMICAL FORMULA: C8H10

*STRUCTURAL FORMULA:

*WLN: 2R

*SYNONYMS:
  EB
  ETHYLBENZOL
  PHENYLETHANE
  NCI C56393

-PHYSICAL CHEMICAL DATA
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*PHYSICAL DESCRIPTIONS: LITERATURE: Clear, colorless liquid
                         REPOSITORY: Clear, colorless liquid

*MOLECULAR WEIGHT: 106.16

*SPECIFIC GRAVITY: 0.867 @ 20/4 C

*DENSITY: 0.866 g/cm3 @ 21 C (RAD)

*MP (DEG C): -95 C

*BP (DEG C): 136.2 C

*SOLUBILITIES:
       WATER : <1 mg/mL @ 23 C (RAD)

        DMSO : >=100 mg/mL @ 23 C (RAD)

 95% ETHANOL : 1-10 mg/mL @ 23 C (RAD)

    METHANOL : Not available

     ACETONE : >=100 mg/mL @ 23 C (RAD)

     TOLUENE : Not available

 OTHER SOLVENTS:
  Most organic solvents: Soluble
  Carbon tetrachloride: Soluble
  Sulfur dioxide: Soluble

Ammonia: Insoluble
ETHER : Soluble
BENZENE: Soluble

*VOLATILITY:
Vapor pressure: 10 mm Hg @ 29.5 C; 5 mm Hg @ 13.9 C; 760 mm Hg @ 136.2 C
Vapor density : 3.66

*FLAMMABILITY(FLASH POINT):
The flash point for this chemical is 15 C (59 F). It is flammable. Fires involving this compound can be controlled with a dry chemical, carbon dioxide or Halon extinguisher. The autoignition temperature is 432 C (810 F).

*UEL: 6.8% LEL: 1.2%

*REACTIVITY:
This compound can react vigorously with strong oxidizing materials.

*STABILITY:
This chemical is stable under normal laboratory conditions. Solutions of this chemical should be stable for 24 hours under normal lab conditions (RAD).

*OTHER PHYSICAL DATA:
Aromatic odor
Refractive index: 1.49594 @ 20 C; 1.4932 @ 25 C
Specific heat: 0.41 cal/gal/degrees C
Viscosity: 0.64 centipoise @ 25 C
Specific gravity: 0.866 @ 25/25 C
Boiling point: 25.8 C @ 10 mm Hg

-TOXICITY
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*NIOSH REGISTRY NUMBER: DA0700000

*TOXICITY:

typ. dose	mode	specie	amount	unit	other
TCLo	ihl	hmn	100	ppm/8H	
LD50	orl	rat	3500	mg/kg	
LCLo	ihl	rat	4000	ppm/4H	
LD50	skn	rbt	17800	mg/kg	
LCLo	ihl	gpg	10000	ppm	

*AQTX/TLM96: 100-10 ppm.

*SAX TOXICITY EVALUATION:
THR: MODERATE via irritation to the skin, eyes and mucous membranes, and via oral and inhalation routes. A concentration of 0.19% vapor in air will irritate eyes; 0.2% is extremely irritating. An experimental teratogen.

*CARCINOGENICITY:
Status: NTP Carcinogenesis Studies; selected but deferred, April 1984

*MUTATION DATA:

test	lowest dose
sce-hmn:lym	1 mmol/L

*TERATOGENICITY:
Reproductive Effects Data:

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    TCLo: ihl-rat   97 ppm/7H (15D preg)
    TCLo: ihl-rat  985 ppm/7H (1-19D preg)
    TCLo: ihl-rat   96 ppm/7H (1-19D preg)
    TCLo: ihl-rbt   99 ppm/7H (1-18D preg)

*STANDARDS, REGULATIONS & RECOMMENDATIONS:
  OSHA: Federal Register (1/19/89) and 29 CFR 1910.1000 Subpart Z
        Transitional Limit: PEL-TWA 100 ppm [610]
        Final Limit: PEL-TWA 100 ppm, STEL 125 ppm [610]
  ACGIH: TLV-TWA 100 ppm, STEL 125 ppm [610]
  NIOSH Criteria Document: None
  NFPA Hazard Rating: Health (H): 2
                      Flammability (F): 3
                      Reactivity (R): 0
  H2: Materials hazardous to health, but areas may be entered freely with
      full-faced mask self-contained breathing apparatus which provides
      eye protection (see NFPA for details).
  F3: Materials which can be ignited under almost all normal temperature
      conditions (see NFPA for details).
  R0: Materials which are normally stable even under fire exposure conditions
      and which are not reactive with water (see NFPA for details).

*OTHER TOXICITY DATA:
  Skin and Eye Irritation Data:
    skn-rbt   15 mg/24H open MLD
    eye-rbt  100 mg
  Standards and Regulations: DOT-Hazard: Flammable liquid; Label: Flammable
                              liquid
  Status: "NIOSH Manual of Analytical Methods, 3rd. Ed."
          Reported in EPA TSCA Inventory, 1983
          EPA TSCA 8(a) Preliminary Assessment Information Final Rule
          EPA Genetic Toxicology Program, January 1984
          EPA TSCA Section 8(e) Status Report 8EHQ-0680-0345
          EPA TSCA Section 8(e) Status Report 8EHQ-1080-0368
          Meets criteria for proposed OSHA Medical Records Rule


-OTHER DATA (Regulatory)
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*PROPER SHIPPING NAME (IATA): Ethylbenzene

*UN/ID NUMBER: UN1175

*HAZARD CLASS: 3             SUBSIDIARY RISK: None    PACKING GROUP: II

*LABELS REQUIRED: Flammable liquid

*PACKAGING: PASSENGER: PKG. INSTR.: 305, Y305       MAXIMUM QUANTITY: 5 L, 1 L
            CARGO    : PKG. INSTR.: 307             MAXIMUM QUANTITY: 60 L

*SPECIAL PROVISIONS: None

*USES:
  Intermediate in production of styrene; organic synthesis; solvent; dilutant;
  antiknock agent; acetophenone manufacture; asphalt constituent; naphtha con-
  stituent.


-HANDLING PROCEDURES
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*ACUTE/CHRONIC HAZARDS:
This compound can cause irritation of the skin, eyes and mucous membranes. It is toxic by ingestion, inhalation and skin absorption. In high concentrations it may be narcotic. It may also cause lachrimation.

*MINIMUM PROTECTIVE CLOTHING: Not available

*RECOMMENDED GLOVE MATERIALS: P
The following gloves show the best resistance based on permeation testing. It is recommended that two different glove types be used for best protection. However, if this chemical makes direct contact with your glove, or if a tear, puncture or hole develops, remove them at once.

SUGGESTED GLOVES (RAD): Viton

*RECOMMENDED RESPIRATOR:
Where the neat test chemical is weighed and diluted, wear a NIOSH-approved half face respirator equipped with an organic vapor/acid gas cartridge (specific for organic vapors, HCl, acid gas and SO2) with a dust/mist filter.

*OTHER: Not available

*STORAGE PRECAUTIONS:
You should store this chemical under refrigerated temperatures, and keep it away from oxidizing materials. STORE AWAY FROM SOURCES OF IGNITION.

*SPILLS AND LEAKAGE:
If you should spill this chemical, FIRST REMOVE ALL SOURCES OF IGNITION, then use absorbent paper to pick up all liquid spill material. Your contaminated clothing and absorbent paper should be sealed in a vapor-tight plastic bag for eventual disposal. Solvent wash all contaminated surfaces with acetone followed by washing with a soap and water solution. Do not reenter the contaminated area until the Safety Officer (or other responsible person) has verified that the area has been properly cleaned.

*DISPOSAL AND WASTE TREATMENT:
Not available

-EMERGENCY PROCEDURES
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*SKIN CONTACT:
IMMEDIATELY flood affected skin with water while removing and isolating all contaminated clothing. Gently wash all affected skin areas thoroughly with soap and water.
If symptoms such as redness or irritation develop, IMMEDIATELY call a physician and be prepared to transport the victim to a hospital for treatment.

*INHALATION:
IMMEDIATELY leave the contaminated area; take deep breaths of fresh air. If symptoms (such as wheezing, coughing, shortness of breath, or burning in the mouth, throat, or chest) develop, call a physician and be prepared to transport the victim to a hospital.
Provide proper respiratory protection to rescuers entering an unknown atmosphere. Whenever possible, Self-Contained Breathing Apparatus (SCBA) should be used; if not available, use a level of protection greater than or equal to that advised under Respirator Recommendation.

*EYE CONTACT:
First check the victim for contact lenses and remove if present. Flush victim's eyes with water or normal saline solution for 20 to 30 minutes while simultaneously calling a hospital or poison control center.
Do not put any ointments, oils, or medication in the victim's eyes without specific instructions from a physician.
IMMEDIATELY transport the victim after flushing eyes to a hospital even if no symptoms (such as redness or irritation) develop.

*INGESTION:
DO NOT INDUCE VOMITING. If the victim is conscious and not convulsing, give 1 or 2 glasses of water to dilute the chemical and IMMEDIATELY call a hospital or poison control center. Be prepared to transport the victim to a hospital if advised by a physician.
If the victim is convulsing or unconscious, do not give anything by mouth, ensure that the victim's airway is open and lay the victim on his/her side with the head lower than the body. DO NOT INDUCE VOMITING. IMMEDIATELY transport the victim to a hospital.

*SYMPTOMS:
Symptoms of exposure to this compound may include irritation, redness and inflammation of the skin; irritation of the nose, throat, and eyes; lachrimation, conjunctivitis, corneal erosion, dermatitis, dizziness, narcosis and a sensation of constriction of the chest.

*FIREFIGHTING:

-SOURCES
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New Jersey Department of Health and Senior Services

HAZARDOUS SUBSTANCE FACT SHEET

Common Name: **ETHYL BENZENE**

CAS Number: 100-41-4
DOT Number: UN 1175

RTK Substance number: 0851
Date: March 1989 Revision: February 1996

HAZARD SUMMARY

* **Ethyl Benzene** can affect you when breathed in and by passing through your skin.
* **Ethyl Benzene** may cause mutations. Handle with extreme caution.
* **Ethyl Benzene** can irritate the eyes, nose and throat.
* Contact with **Ethyl Benzene** can irritate the skin. Prolonged exposure can cause drying, scaling and even blistering.
* Exposure to high concentrations can cause you to become dizzy, lightheaded, and to pass out. Very high levels can cause trouble breathing and even death.
* High exposure may damage the liver.
* **Ethyl Benzene** is a FLAMMABLE LIQUID and a FIRE HAZARD.

IDENTIFICATION

Ethyl Benzene is a colorless liquid with an aromatic odor. It is used in the production of *styrene* and synthetic polymers, as a solvent and as a component of automotive and aviation fuels.

REASON FOR CITATION

* **Ethyl Benzene** is on the Hazardous Substance List because it is regulated by OSHA and cited by ACGIH, DOT, DEP, NIOSH, NFPA, HHAG and EPA.
* This chemical is on the Special Health Hazard Substance List because it is **FLAMMABLE**.
* Definitions are provided on page 5.

HOW TO DETERMINE IF YOU ARE BEING EXPOSED

The New Jersey Right to Know Act requires most employers to label chemicals in the workplace and requires public employers to provide their employees with information and training concerning chemical hazards and controls. The federal OSHA Hazard Communication Standard, 1910.1200, requires private employers to provide similar training and information to their employees.

* Exposure to hazardous substances should be routinely evaluated. This may include collecting air samples. Under OSHA 1910.20, you have a legal right to obtain copies of sampling results from your employer. If you think you are experiencing any work-related health problems, see a doctor trained to recognize occupational diseases. Take this Fact Sheet with you.
* **ODOR THRESHOLD = 0.092-0.60 ppm**.
* The range of accepted odor threshold values is quite broad. Caution should be used in relying on odor alone as a warning of potentially hazardous exposures.

WORKPLACE EXPOSURE LIMITS

OSHA: The legal airborne permissible exposure limit (PEL) is **100 ppm** averaged over an 8-hour workshift.

NIOSH: The recommended airborne exposure limit is **100 ppm** averaged over a 10-hour workshift.

ACGIH: The recommended airborne exposure limit is **100 ppm** averaged over an 8-hour workshift and **125 ppm** as a STEL (short term exposure limit).

* **Ethyl Benzene** may cause mutations. All contact with this chemical should be reduced to the lowest possible level.
* The above exposure limits are for air levels only. When skin contact also occurs, you may be overexposed, even though air levels are less than the limits listed above.

WAYS OF REDUCING EXPOSURE

* Where possible, enclose operations and use local exhaust ventilation at the site of chemical release. If local exhaust ventilation or enclosure is not used, respirators should be worn.
* Wear protective work clothing.
* Wash thoroughly immediately after exposure to **Ethyl Benzene** and at the end of the workshift.
* Post hazard and warning information in the work area. In addition, as part of an ongoing education and training effort, communicate all information on the health and safety hazards of **Ethyl Benzene** to potentially exposed workers.

This Fact Sheet is a summary source of information of all potential and most severe health hazards that may result from exposure. Duration of exposure, concentration of the substance and other factors will affect your susceptibility to any of the potential effects described below.

HEALTH HAZARD INFORMATION

Acute Health Effects

The following acute (short-term) health effects may occur immediately or shortly after exposure to **Ethyl Benzene**:

* **Ethyl Benzene** can irritate the eyes, nose and throat.
* Contact with **Ethyl Benzene** can irritate the skin.
* Exposure to high concentrations can cause you to become dizzy, lightheaded and to pass out. Very high levels can cause trouble breathing and even death.

Chronic Health Effects

The following chronic (long-term) health effects can occur at some time after exposure to **Ethyl Benzene** and can last for months or years:

Cancer Hazard

* **Ethyl Benzene** may cause mutations (genetic changes). Whether or not it poses a cancer or reproductive hazard needs further study.

Reproductive Hazard

* There is limited evidence that **Ethyl Benzene** may damage the developing fetus.

Other Long-Term Effects

* Prolonged exposure can cause drying, scaling and even blistering of the skin
* High exposure may damage the liver.
* This chemical has not been adequately evaluated to determine whether brain or other nerve damage could occur with repeated exposure. However, many solvents and other petroleum-based chemicals have been shown to cause such damage. Effects may include reduced memory and concentration, personality changes (withdrawal, irritability), fatigue, sleep disturbances, reduced coordination, and/or effects on nerves supplying internal organs (autonomic nerves) and/or nerves to the arms and legs (weakness, "pins and needles").

MEDICAL

Medical Testing

If symptoms develop or overexposure is suspected, the following may be useful:

* Liver function tests.

Evaluate for brain effects such as changes in memory, concentration, sleeping patterns and mood (especially irritability and social withdrawal), as well as headaches and fatigue. Consider evaluations of the cerebellar, autonomic and peripheral nervous systems. Positive and borderline individuals should be referred for neuropsychological testing.

Any evaluation should include a careful history of past and present symptoms with an exam. Medical tests that look for damage already done are not a substitute for controlling exposure.

Request copies of your medical testing. You have a legal right to this information under OSHA 1910.20.

WORKPLACE CONTROLS AND PRACTICES

Unless a less toxic chemical can be substituted for a hazardous substance, **ENGINEERING CONTROLS** are the most effective way of reducing exposure. The best protection is to enclose operations and/or provide local exhaust ventilation at the site of chemical release. Isolating operations can also reduce exposure. Using respirators or protective equipment is less effective than the controls mentioned above, but is sometimes necessary.

In evaluating the controls present in your workplace, consider: (1) how hazardous the substance is, (2) how much of the substance is released into the workplace and (3) whether harmful skin or eye contact could occur. Special controls should be in place for highly toxic chemicals or when significant skin, eye, or breathing exposures are possible.

In addition, the following controls are recommended:

* Where possible, automatically pump liquid **Ethyl Benzene** from drums or other storage containers to process containers.
* Before entering a confined space where **Ethyl Benzene** may be present, check to make sure that an explosive concentration does not exist.

Good **WORK PRACTICES** can help to reduce hazardous exposures. The following work practices are recommended:

* Workers whose clothing has been contaminated by **Ethyl Benzene** should change into clean clothing promptly.
* Contaminated work clothes should be laundered by individuals who have been informed of the hazards of exposure to **Ethyl Benzene**.
* Eye wash fountains should be provided in the immediate work area for emergency use.
* If there is the possibility of skin exposure, emergency shower facilities should be provided.

* On skin contact with **Ethyl Benzene**, immediately wash or shower to remove the chemical. At the end of the workshift, wash any areas of the body that may have contacted **Ethyl Benzene**, whether or not known skin contact has occurred.
* Do not eat, smoke, or drink where **Ethyl Benzene** is handled, processed, or stored, since the chemical can be swallowed. Wash hands carefully before eating or smoking.

PERSONAL PROTECTIVE EQUIPMENT

WORKPLACE CONTROLS ARE BETTER THAN PERSONAL PROTECTIVE EQUIPMENT. However, for some jobs (such as outside work, confined space entry, jobs done only once in a while, or jobs done while workplace controls are being installed), personal protective equipment may be appropriate.

The following recommendations are only guidelines and may not apply to every situation.

Clothing

* Avoid skin contact with **Ethyl Benzene**. Wear solvent-resistant gloves and clothing. Safety equipment suppliers/ manufacturers can provide recommendations on the most protective glove/clothing material for your operation.
* All protective clothing (suits, gloves, footwear, headgear) should be clean, available each day, and put on before work.

Eye Protection

* Wear splash-proof chemical goggles and face shield when working with liquid, unless full facepiece respiratory protection is worn.

Respiratory Protection

IMPROPER USE OF RESPIRATORS IS DANGEROUS. Such equipment should only be used if the employer has a written program that takes into account workplace conditions, requirements for worker training, respirator fit testing and medical exams, as described in OSHA 1910.134.

* Where the potential exists for exposures over **100 ppm**, use a MSHA/NIOSH approved respirator with an organic vapor cartridge/canister. More protection is provided by a full facepiece respirator than by a half-mask respirator, and even greater protection is provided by a powered-air purifying respirator.
* If while wearing a filter, cartridge or canister respirator, you can smell, taste, or otherwise detect **Ethyl Benzene**, or in the case of a full facepiece respirator you experience eye irritation, leave the area immediately. Check to make sure the respirator-to-face seal is still good. If it is, replace the filter, cartridge, or canister. If the seal is no longer good, you may need a new respirator.
* Be sure to consider all potential exposures in your workplace. You may need a combination of filters, prefilters, cartridges, or canisters to protect against different forms of a chemical (such as vapor and mist) or against a mixture of chemicals.
* Where the potential for high exposures exists, use a MSHA/NIOSH approved supplied-air respirator with a full facepiece operated in the positive pressure mode or with a full facepiece, hood, or helmet in the continuous flow mode, or use a MSHA/NIOSH approved self-contained breathing apparatus with a full facepiece operated in pressure-demand or other positive pressure mode.
* Exposure to **800 ppm** is immediately dangerous to life and health. If the possibility of exposures above **800 ppm** exists, use a MSHA/NIOSH approved self-contained breathing apparatus with a full facepiece operated in continuous flow or other positive pressure mode.

QUESTIONS AND ANSWERS

Q: If I have acute health effects, will I later get chronic health effects?

A: Not always. Most chronic (long-term) effects result from repeated exposures to a chemical.

Q: Can I get long-term effects without ever having short-term effects?

A: Yes, because long-term effects can occur from repeated exposures to a chemical at levels not high enough to make you immediately sick.

Q: What are my chances of getting sick when I have been exposed to chemicals?

A: The likelihood of becoming sick from chemicals is increased as the amount of exposure increases. This is determined by the length of time and the amount of material to which someone is exposed.

Q: When are higher exposures more likely?
A: Conditions which increase risk of exposure include physical and mechanical processes (heating, pouring, spraying, spills and evaporation from large surface areas such as open containers), and "confined space" exposures (working inside vats, reactors, boilers, small rooms, etc.).

Q: Is the risk of getting sick higher for workers than for community residents?
A: Yes. Exposures in the community, except possibly in cases of fires or spills, are usually much lower than those found in the workplace. However, people in the community may be exposed to contaminated water as well as to chemicals in the air over long periods. Because of this, and because of exposure of children or people who are already ill, community exposures may cause health problems.

Q: Who is at the greatest risk from reproductive hazards?
A: Pregnant women are at greatest risk from chemicals that harm the developing fetus. However, chemicals may affect the ability to have children, so both men and women of childbearing age are at high risk.

Q: Can men as well as women be affected by chemicals that cause reproductive system damage?
A: Yes. Some chemicals reduce potency or fertility in both men and women. Some damage sperm and eggs, possibly leading to birth defects.

The following information is available from:

New Jersey Department of Health and
Senior Services
Occupational Disease and Injury Services
Trenton, NJ 08625-0360
(609) 984-1863

Industrial Hygiene Information

Industrial hygienists are available to answer your questions regarding the control of chemical exposures using exhaust ventilation, special work practices, good housekeeping, good hygiene practices, and personal protective equipment including respirators. In addition, they can help to interpret the results of industrial hygiene survey data.

Medical Evaluation

If you think you are becoming sick because of exposure to chemicals at your workplace, you may call a Department of Health and Senior Services physician who can help you find the services you need.

Public Presentations

Presentations and educational programs on occupational health or the Right to Know Act can be organized for labor unions, trade associations and other groups.

Right to Know Information Resources

The Right to Know Infoline (609) 984-2202 can answer questions about the identity and potential health effects of chemicals, list of educational materials in occupational health, references used to prepare the Fact Sheets, preparation of the Right to Know survey, education and training programs, labeling requirements, and general information regarding the Right to Know Act. Violations of the law should be reported to (609) 984-2202.

DEFINITIONS

ACGIH is the American Conference of Governmental Industrial Hygienists. It recommends upper limits (called TLVs) for exposure to workplace chemicals.

A **carcinogen** is a substance that causes cancer.

The **CAS number** is assigned by the Chemical Abstracts Service to identify a specific chemical.

A **combustible** substance is a solid, liquid or gas that will burn.

A **corrosive** substance is a gas, liquid or solid that causes irreversible damage to human tissue or containers.

DEP is the New Jersey Department of Environmental Protection.

DOT is the Department of Transportation, the federal agency that regulates the transportation of chemicals.

EPA is the Environmental Protection Agency, the federal agency responsible for regulating environmental hazards.

A **fetus** is an unborn human or animal.

A **flammable** substance is a solid, liquid, vapor or gas that will ignite easily and burn rapidly.

The **flash point** is the temperature at which a liquid or solid gives off vapor that can form a flammable mixture with air.

HHAG is the Human Health Assessment Group of the federal EPA.

IARC is the International Agency for Research on Cancer, a scientific group that classifies chemicals according to their cancer-causing potential.

A **miscible** substance is a liquid or gas that will evenly dissolve in another.

mg/m^3 means milligrams of a chemical in a cubic meter of air. It is a measure of concentration (weight/volume).

MSHA is the Mine Safety and Health Administration, the federal agency that regulates mining. It also evaluates and approves respirators.

A **mutagen** is a substance that causes mutations. A **mutation** is a change in the genetic material in a body cell. Mutations can lead to birth defects, miscarriages, or cancer.

NAERG is the North American Emergency Response Guidebook. It was jointly developed by Transport Canada, the United States Department of Transportation and the Secretariat of Communications and Transportation of Mexico. It is a guide for first responders to quickly identify the specific or generic hazards of material involved in a transportation incident, and to protect themselves and the general public during the initial response phase of the incident.

NCI is the National Cancer Institute, a federal agency that determines the cancer-causing potential of chemicals.

NFPA is the National Fire Protection Association. It classifies substances according to their fire and explosion hazard.

NIOSH is the National Institute for Occupational Safety and Health. It tests equipment, evaluates and approves respirators, conducts studies of workplace hazards, and proposes standards to OSHA.

NTP is the National Toxicology Program which tests chemicals and reviews evidence for cancer.

OSHA is the Occupational Safety and Health Administration, which adopts and enforces health and safety standards.

PEOSHA is the Public Employees Occupational Safety and Health Act, a state law which sets PELs for New Jersey public employees.

ppm means parts of a substance per million parts of air. It is a measure of concentration by volume in air.

A **reactive** substance is a solid, liquid or gas that releases energy under certain conditions.

A **teratogen** is a substance that causes birth defects by damaging the fetus.

TLV is the Threshold Limit Value, the workplace exposure limit recommended by ACGIH.

The **vapor pressure** is a measure of how readily a liquid or a solid mixes with air at its surface. A higher vapor pressure indicates a higher concentration of the substance in air and therefore increases the likelihood of breathing it in.

>>>>>>>>>>>>>>>> **E M E R G E N C Y I N F O R M A T I O N** <<<<<<<<<<<<<<<<

Common Name: **ETHYL BENZENE**
DOT Number: **UN 1175**
NAERG Code: **129**
CAS Number: **100-41-4**

Hazard rating	NJDHSS	NFPA
FLAMMABILITY	-	3
REACTIVITY	-	0
POISONOUS GASES ARE PRODUCED IN FIRE CONTAINERS MAY EXPLODE IN FIRE		

Hazard Rating Key: 0=minimal; 1=slight; 2=moderate; 3=serious; 4=severe

FIRE HAZARDS

* **Ethyl Benzene** is a FLAMMABLE LIQUID.
* Use dry chemical, CO_2, water spray, or alcohol resistant foam extinguishers.
* POISONOUS GASES ARE PRODUCED IN FIRE.
* CONTAINERS MAY EXPLODE IN FIRE.
* Vapors may travel to a source of ignition and flash back.
* If employees are expected to fight fires, they must be trained and equipped as stated in OSHA 1910.156.

SPILLS AND EMERGENCIES

If **Ethyl Benzene** is spilled or leaked, take the following steps:

* Restrict persons not wearing protective equipment from area of spill or leak until clean-up is complete.
* Remove all ignition sources.
* Ventilate area of spill or leak.
* It may be necessary to contain and dispose of **Ethyl Benzene** as a HAZARDOUS WASTE. Contact your Department of Environmental Protection (DEP) or your regional office of the federal Environmental Protection Agency (EPA) for specific recommendations.
* If employees are required to clean-up spills, they must be properly trained and equipped. OSHA 1910.120(q) may be applicable.

==========

FOR LARGE SPILLS AND FIRES immediately call your fire department. You can request emergency information from the following:

CHEMTREC: (800) 424-9300
NJDEP HOTLINE: (609) 292-7172

==========

HANDLING AND STORAGE

* Prior to working with **Ethyl Benzene** you should be trained on its proper handling and storage.
* **Ethyl Benzene** must be stored to avoid contact with STRONG OXIDIZERS since violent reactions occur.
* Sources of ignition, such as smoking and open flames, are prohibited where **Ethyl Benzene** is handled, used, or stored.
* Metal containers involving the transfer of **Ethyl Benzene** should be grounded and bonded. Drums must be equipped with self-closing valves, pressure vacuum bungs, and flame arresters.
* Use only non-sparking tools and equipment, especially when opening and closing containers of **Ethyl Benzene**.

FIRST AID

IN NJ, POISON INFORMATION 1-800-962-1253

Eye Contact
* Immediately flush with large amounts of water for at least 15 minutes, occasionally lifting upper and lower lids.

Skin Contact
* Quickly remove contaminated clothing. Immediately wash contaminated skin with large amounts of soap and water.

Breathing
* Remove the person from exposure.
* Begin rescue breathing if breathing has stopped and CPR if heart action has stopped.
* Transfer promptly to a medical facility.

PHYSICAL DATA

Vapor Pressure: 7.1 mmHg at 68^{o}F (20^{o}C)
Flash Point: 55^{o}F (12.8^{o}C)
Water Solubility: Slightly soluble

OTHER COMMONLY USED NAMES

Chemical Name:
Benzene, Ethyl-
Other Names:
Ethylbenzol; Phenylethane

Not intended to be copied and sold for commercial purposes.

NEW JERSEY DEPARTMENT OF HEALTH AND
SENIOR SERVICES
Right to Know Program
PO Box 368, Trenton, NJ 08625-0368
(609) 984-2202

Web Sites

that offer searchable chemical databases, recommended by Scorecard

---

If you want more detailed information about a chemical than Scorecard provides, there are several on-line and library resources Scorecard recommends for further research.

ON-LINE CHEMICAL DATABASES

CambridgeSoft Chemfinder
http://chemfinder.camsoft.com/

Search

Chemfinder gives basic physico-chemical data and molecular structures for chemicals, and provides links to international data sources addressing specific chemicals.

Hazardous Substances Data Bank
http://toxnet.nlm.nih.gov/

Search

HSDB focuses on the toxicology of potentially hazardous chemicals, and includes peer-reviewed information on human exposure, industrial hygiene, emergency handling procedures, environmental fate, and regulatory requirements.

University of Akron Hazardous Chemicals Database
http://ull.chemistry.uakron.edu/erd/

Search

The Hazardous Chemicals Database provides physical data on chemicals and links to Department of Transportation safety guides that are valuable for emergency response.

BIBLIOGRAPHIC RESOURCES ON CHEMICAL TOXICITY

Scorecard provides qualitative summaries of the health hazards posed by a chemical (e.g., it is a suspected neurotoxicant), but not direct access to supporting toxicological data. These scientific studies are abstracted in several toxicity databases, which are available in libraries, from commercial vendors, and sometimes on-line. The major toxicity databases include:

The Registry of Toxic Effects of Chemicals Substances (RTECS)
RTECS is a database of toxicological information compiled by the National Institute for Occupational Safety and Health. It contains summary information about the types of health effects chemicals can cause and the concentrations at which toxicity is known to occur. It is available from several commercial vendors at http://www.cdc.gov/niosh/rtecs.html, and can often be found at major public or university libraries.

TOXLINE
Free access to the National Library of Medicine's toxicology-specific database of abstracts, reference journal articles, and reports is available at http://www.medscape.com/misc/FormToxlineInfLive.html

MEDLINE

Free access to the National Library of Medicine's MEDLINE database of more than 9 million references to articles published in 3800 biomedical journals is available at http://www.nlm.nih.gov/databases/freemedl.html. Two Web-based products, PubMed and Internet Grateful Med, provide this access. Medline can also be accessed at http://www.medscape.com/misc/FormMedlineInfLive.html

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SOLVENT NAPHTHA (PETROLEUM), LIGHT ALIPHATIC (64742-89-8)

summary from the About the Chemicals section of Scorecard

- **Human Health Hazards** **Reference(s)**

  Recognized: --

  Suspected: --

- **Hazard Rankings**

  Data lacking; not ranked by any system in Scorecard.

- **Chemical Use Profile**

  This is a high volume chemical with production exceeding 1 million pounds annually in the U.S.

  No data on industrial use in Scorecard.

  Used in consumer products, building materials or furnishings that contribute to indoor air pollution.

- **Profile of Environmental Release and Waste Generation**

  No data on environmental releases in Scorecard.

- **Regulatory Coverage**

  Not on chemical lists in Scorecard.

- **Basic Testing to Identify Chemical Hazards**

  6 of 8 basic tests to identify chemical hazards have not been conducted on this chemical, or are not publicly available.

- **Information Needed for Safety Assessment**

  Lacks at least some of the national data required for safety assessment.

  No data on risk assessment values in Scorecard.

- **Links**

  Other web sites specific to this chemical:

  If none of these sources meet your needs, you can try searching some other chemical database Web sites.

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Consumer Products

that contain SOLVENT NAPHTHA (PETROLEUM), LIGHT ALIPHATIC (64742-89-8) from Scorecard

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What kinds of consumer products may contain this chemical?

- Aerosol paint concentrates

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Basic Testing to Identify Chemical Hazards

for SOLVENT NAPHTHA (PETROLEUM), LIGHT ALIPHATIC (64742-89-8) from Scorecard

---

The U.S. EPA conducted a comprehensive review of publicly available chemical testing data in 1997 to examine whether the basic information needed to identify chemical hazards is available for high production volume chemicals. EPA searched major chemical databases to determine if the following tests had been conducted on a chemical:

- Acute toxicity
- Chronic toxicity
- Neurotoxicity
- Developmental or reproductive toxicity
- Mutagenicity
- Carcinogenicity
- Ecotoxicity
- Environmental fate

The following basic tests to identify chemical hazards have either not been conducted or are not publicly available:

- Carcinogenicity
- Chronic toxicity
- Developmental or reproductive toxicity
- Ecotoxicity
- Environmental fate
- Neurotoxicity

More on the importance of basic toxicity testing

Reference

EPA. Chemical Hazard Data Availability Study: High Production Volume (HPV) Chemicals and SIDS Testing
Office of Pollution Prevention and Toxics, EPA,Washington, DC. 1998.

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Safety Assessment Data

for SOLVENT NAPHTHA (PETROLEUM), LIGHT ALIPHATIC (64742-89-8) from Scorecard

---

Are Risk Assessment Values Available?

Health Risk of Concern	Inhalation	Ingestion
Cancer	Not a recognized carcinogen	Not a recognized carcinogen
Noncancer	**No**	**No**

Are Exposure Data Available?

Type of Exposure	
Inhalation - ambient air	**No**
Inhalation - indoor air	**No**
Ingestion	**No**

- See the data US EPA possesses for safety assessment.

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Web Sites

that offer searchable chemical databases, recommended by Scorecard

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1 Synonyms
2 Synonyms
3 Synonyms
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Select Clear

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Non-Human Toxicity Excerpts
Non-Human Toxicity Values
Ecotoxicity Values
Metabolism/Pharmacokinetics

ETHYL ACETATE

CASRN: 141-78-6

For other data, click on the Table of Contents

Best Sections

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PEER REVIEWED

Synonyms :

VINEGAR NAPHTHA
PEER REVIEWED

Synonyms :

Aethylacetat (German)
PEER REVIEWED

Synonyms :

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PEER REVIEWED

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National Toxicology Program Studies

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Best Sections

Metabolism/Metabolites :

The purpose of this study was to clarify whether the blood concentration of inhaled toluene, ethylbenzene, m-xylene, or mesitylene can change after the concomitant pulmonary absorption of **ethyl acetate. (**Adult female Sprague-Dawley rats were exposed in a 20 liter glass chamber under dynamic conditions for 2 hours to various concentrations of the aromatics without or in combination with different concentrations of **ethyl acetate (**0, 1000, or 4000 ppm) in air. Concentration ranges were as follows: toluene, 140-690 ppm; ethylbenzene, 120-650 ppm; m-xylene, 100-560 ppm; mesitylene, 120-720 ppm; and **ethyl acetate,** 1000 or 4000 ppm. The coexposures with **ethyl acetate** lowered the blood concentrations of other inhaled aromatics. This reduction was statistically significant following a 2 hour exposure to 230 ppm toluene in combination with 1000 ppm **ethyl acetate,** 650 ppm ethylbenzene with 1000 ppm **ethyl acetate,** and 100 ppm m-xylene with 4000 ppm **ethyl acetate.)** Similarly a significant reduction of the blood level of the aromatics by **ethyl acetate** coinhalation was also observed at higher exposure concentrations with toluene and m-xylene. A metabolic interaction such as enhanced disposition of the aromatics, may be responsible for these effects. However, it is possible that the solubility of the solvents could be altered by the presence of **ethyl acetate.** It was concluded that coexposures to concentrations in the order of the threshold limit values (100 ppm for these solvents) with 400 ppm **ethyl acetate** should not be followed by a dangerous change of the blood levels of the aromatics.
[Freundt KJ et al; Bull Environ Contam Toxicol 42 (4): 495-8 (1989)]**PEER REVIEWED**

- ☐ Non-Human Toxicity Values
- ☐ Ecotoxicity Values
- ☐ TSCA Test Submissions
- ☐ Metabolism/Pharmacokinetics
- ☐ Metabolism/Metabolites
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HSDB Search Results

for ETHYL ACETATE 141-78-6

Information added from CHEMID:
Chemid Name: **ethyl acetate [141-78-6]**
(vinegar naphtha, octan etylu, ethylacetaat, ethyl ethanoate, essigester, aethylacetat, acetoxyethane, acetidin, acetic ether)
ethyl acetate (vinegar naphtha, octan etylu, ethylacetaat, ethyl ethanoate, essigester, aethylacetat, acetoxyethane, acetidin, acetic ether)

Query:

Registry Numbers:
141-78-6 141-78-6
~
1 record contains the exact substance name or CAS registry number.
362 records contain all of the query terms anywhere in the record.

Items **1** through **20** of **363** **Pages:** **1** 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19

*Substance Names are sorted in **relevancy ranked** order.*

	Substance Name

The following is the primary record for the chemical. All of the query terms were found.

1	**ETHYL ACETATE** 141-78-6

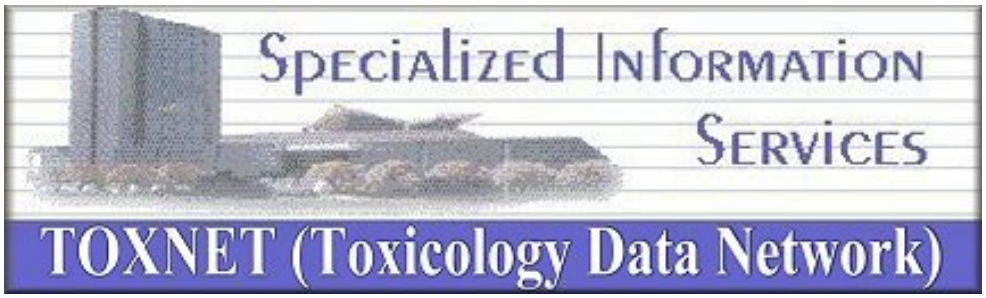
The following 362 records contain one or more of the requested chemical name(s) and all of the query terms anywhere in the record.

2	**ETHYLBENZENE** 100-41-4
3	**ETHANOL** 64-17-5
4	**N-AMYL ACETATE** 628-63-7
5	**N-BUTYL ACETATE** 123-86-4
6	**1-METHYL-2-PYRROLIDINONE** 872-50-4

7	**TRIGLYCOL DIACETATE** 111-21-7
8	**ETHYL N-BUTYRATE** 105-54-4
9	**ISOAMYL ACETATE** 123-92-2
10	**ETHYL LACTATE** 97-64-3
11	**CHLORAMPHENICOL** 56-75-7
12	**CHLORMEPHOS** 24934-91-6
13	**T-2 TOXIN** 21259-20-1
14	**2-PYRROLIDONE** 616-45-5
15	**MESITYLENE** 108-67-8
16	**ACETALDEHYDE** 75-07-0
17	**ISOBUTYL ACETATE** 110-19-0
18	**METHYL ISOBUTYL KETONE** 108-10-1
19	**ACETAMIDE** 60-35-5
20	**MITHRAMYCIN** 18378-89-7

Items **1** through **20** of **363** **Pages:** **1** 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19





SEARCH DATABASES
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ChemIDplus
DART/ETIC
EMIC
GENE-TOX
HSDB
HSDB Structures
IRIS
NCI - 3D
TOXLINE
TRI
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Basic Search

HSDB: Hazardous Substances Data Bank

Search in HSDB Records for:

SEARCH CLEAR

Add chemical name searching?

(•) Yes ( ) No

Go To: Custom Search | Browse Index | Help

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For reporting problems, contact: Webmaster

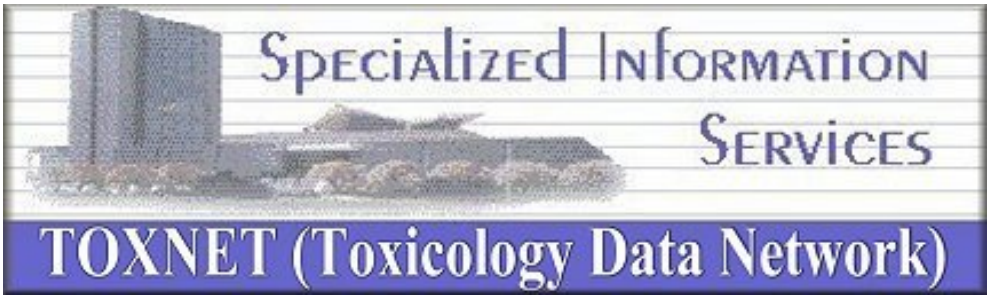
Last Modified **Wed Feb 7 14:34:33 2001**

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ChemIDplus
DART/ETIC
EMIC
GENE-TOX
HSDB
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IRIS
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Custom Search

HSDB: Hazardous Substances Data Bank

SEARCH CLEAR

Help | Browse Index | Basic Search

Search: ○ exact words ◉ singular and plural forms ○ word variants
Select records containing: ○ the phrase ◉ all of the words ○ any of the words

☑ Add chemical name searching.

Limit your search to the following Fields: (If no boxes are checked, all fields will be searched.)

SUBSTANCE IDENTIFICATION			
☐ Chemical Names	☐ CAS Registry Number	☐ Molecular Formula	☐ Molecular Weight
☐ Wiswesser Line Notation	☐ RTECS Number	☐ OHM-TADS Number	☐ Shipping Name/Number
☐ Standard Transportation Number	☐ EPA Hazardous Waste Number	☐ Associated Chemicals	☐ Notes
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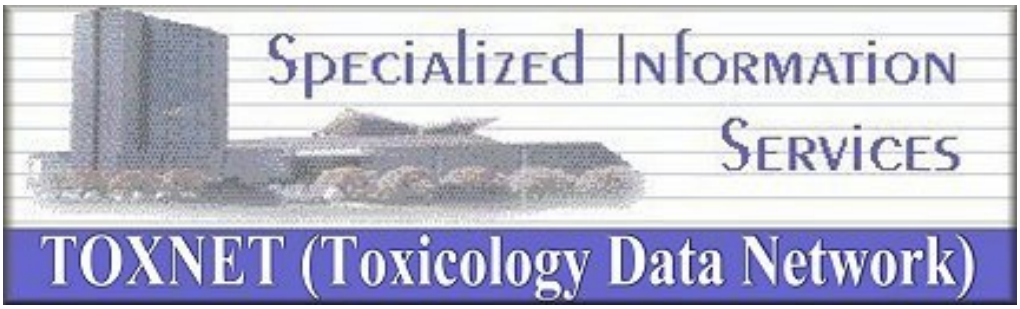
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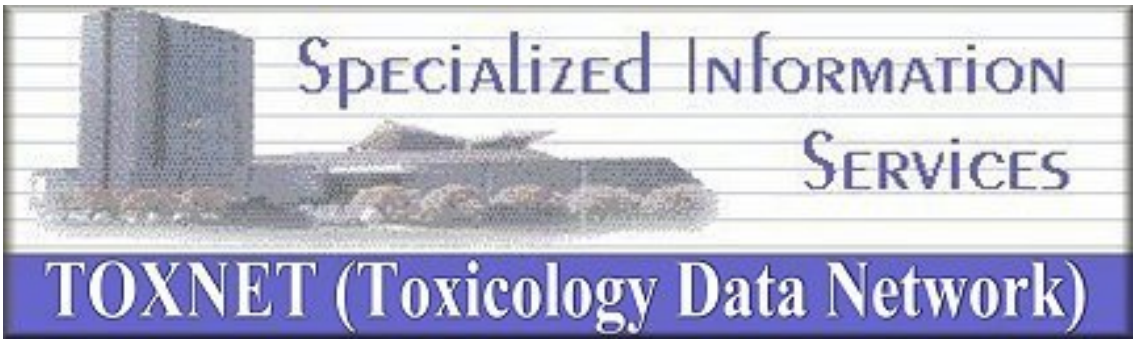
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Welcome to TOXNET - A cluster of databases on toxicology, hazardous chemicals, and related areas. TOXNET NEWS. New: TRI98 now available!

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For **Toxic Release Information** (Annual estimated releases of toxic chemicals to the environment - the Environmental Protection Agency's TRI (Toxics Release Inventory)	
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ETHYL ACETATE

CASRN: 141-78-6

For other data, click on the Table of Contents

Synonyms:

ESSIGESTER (GERMAN)

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ETHYL ACETATE

CASRN: 141-78-6

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Synonyms:

VINEGAR NAPHTHA

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ETHYL ACETATE

CASRN: 141-78-6

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Synonyms:

Aethylacetat (German)

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ETHYL ACETATE

CASRN: 141-78-6

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Synonyms:

ETHYLACETAAT (DUTCH)

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ETHYL ACETATE

CASRN: 141-78-6

For other data, click on the Table of Contents

Human Health Effects:

Human Toxicity Excerpts:

STUDY OF 30 WORKERS EXPOSED CHRONICALLY TO 15-50 MG OF **ETHYL ACETATE** IN ADDITION TO 20 TO 80 MG OF AMYL ACETATE/L OF AIR SHOWED NO ... ABNORMALITIES IN CORNEA, MERELY HYPEREMIA OF BULBAR CONJUNCTIVA. ... PROLONGED INHALATION MAY BE DAMAGING TO LUNG, LIVER, KIDNEY, & HEART. ... NO EFFECT ON EYES ... KNOWN FROM SYSTEMIC ABSORPTION.

[Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986. 412]**PEER REVIEWED**

UNACCLIMATED SUBJECTS ... FOUND THE ODOR /OF **ETHYL ACETATE/** OBJECTIONABLY STRONG AT 200 PPM, AND MILD EYE, NOSE, AND THROAT IRRITATION AT 400 PPM.

[American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices. 5th ed. Cincinnati, OH:American Conference of Governmental Industrial Hygienists, 1986. 239]**PEER REVIEWED**

ETHYL ACETATE TESTED AT 10% IN PETROLATUM PRODUCED NO IRRITATION AFTER A 48-HOUR CLOSED PATCH TEST IN 25 HUMAN SUBJECTS. SENSITIZATION: A MAXIMIZATION TEST WAS CARRIED OUT ON 25 VOLUNTEERS. THE MATERIAL WAS TESTED AT A CONCN OF 10% IN PETROLATUM AND PRODUCED NO SENSITIZATION REACTIONS.

[Opdyke, D.L.J. (ed.). Monographs on Fragrance Raw Materials. New York: Pergamon Press, 1979. 341]**PEER REVIEWED**

SYMPTOMATOLOGY (acute intoxication): 1. Early emotional lability: exhilaration, boastfulness, talkativeness, remorse, and belligerency. 2. Impaired motor coordination: slowed reaction time, slurred speech, ataxia. 3. Sensory disturbances: diplopia, vertigo. 4. Flushing of face, rapid pulse, sweating. 5. Nausea and vomiting. Eventual incontinence of urine and feces. 6. Drowsiness, stupor, and finally coma, with impaired or absent tendon reflexes. Convulsive episodes may indicate hypoglycemia. 7. Pupils dilated or normal. 8. Peripheral vascular collapse (shock); hypotension, tachycardia, cold pale skin, hypothermia. 9. Slow stentorous respiration. 10. Death from respiratory or circulatory failure or from aspiration pneumonitis. 11. During convalescence: postalcoholic headache and gastritis; infections, alcoholic psychoses. /Ethyl alcohol/

[Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984.,p. III-169-70]**PEER REVIEWED**

Poison by inhalation. Moderately toxic by intraperitoneal and subcutaneous routes. Mildly toxic by ingestion. Human systemic effects by inhalation: olfactory changes, conjunctiva irritation, and

pulmonary changes. Human eye irritant. Irritating to mucous surfaces ... and is also mildly narcotic. On repeated or prolonged exposures, it causes conjunctival irritation and corneal clouding. High concentrations have a narcotic effect and can cause congestion of the liver and kidneys. Chronic poisoning has been described as producing anemia, leucocytosis (transient increase in the white blood cell count), and cloudy swelling, and fatty degeneration of the viscera.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1514]**PEER REVIEWED**

ETHYL ACETATE HAS ... REPUTATION OF BEING ONE OF THE LEAST TOXIC OF THE VOLATILE ORGANIC SOLVENTS.
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Volumes I,II, III. Cincinnati, OH: ACGIH, 1991. 569]**PEER REVIEWED**

IRRITANT EFFECT OF **ETHYL ACETATE** IS LESS STRONG THAN THAT OF PROPYL ACETATE OR BUTYL ACETATE.
[International Labour Office. Encyclopedia of Occupational Health and Safety. Volumes I and II. New York: McGraw-Hill Book Co., 1971. 477]**PEER REVIEWED**

... ALLEGED ILL EFFECTS OF **ETHYL ACETATE** HAVE OCCURRED DURING ITS INTENSIVE USE DURING EARLIER YEARS ... IMPURITIES MAY HAVE BEEN PRESENT OR IT MAY HAVE BEEN USED WITHOUT DUE CARE AND OFTEN IN COMBINATION WITH OTHER SOLVENTS.
[Snyder, R. (ed.). Ethel Browning's Toxicity and Metabolism of Industrial Solvents. Second Edition. Volume 3 Alcohols and Esters. New York, NY: Elsevier, 1992. 239]**PEER REVIEWED**

THE ALIPHATIC ESTERS USED AS LACQUER SOLVENTS, PRIMARILY **ETHYL ACETATE** AND BUTYL ACETATE, HAVE ... /SRP: CNS DEPRESSANT/ PROPERTIES WHICH ARE LESS PROMINENT THAN THOSE ASSOCIATED WITH THE CHLORINATED HYDROCARBONS.
[Hamilton, A., and H. L. Hardy. Industrial Toxicology. 3rd ed. Acton, Mass.: Publishing Sciences Group, Inc., 1974. 313]**PEER REVIEWED**

/Seventeen/ track team runners were evaluated after complaining of wheezing coughing, rhinitis, or shortness of breath after practicing in a facility under construction. Investigation revealed levels of **ethyl acetate** and toluene low enough to meet federal guidelines but apparently sufficient to cause symptoms in the athletes. Therefore, current standards for regulating potentially toxic organic chemicals may be inadequate when aerobic exercise is performed in the polluted environment.
[Larson DC; Physician Sportsmed 13 (1): 76-79 (1985)]**PEER REVIEWED**

A survey of the uptake of 5-hydroxytryptamine (serotonin) in platelets of workers exposed to organic solvents was conducted. Blood samples were obtained from six males, ages 34 to 58, employed in a graphic paint manufacturing facility and from 50 nonexposed individuals, 25 to 56 years old. Platelets were isolated and incubated with (14)carbon labeled serotonin. The uptake of radiolabeled serotonin, serum concentrations of calcium, potassium, and sodium ions, platelet count, and blood pH were also

determined. Breathing zone concentrations of organic solvents were obtained and analyzed by gas chromatography. The platelet count of the exposed workers was less than that of the comparisons. Maximal uptake rates of serotonin by platelets from the exposed workers was significantly greater than that of the comparisons. No significant differences in blood ion concentrations or pH values in the workers or comparisons were noted. The total concentration of organic solvents in the breathing zones of the exposed subjects ranged from 13 to 111 ppm. Compounds identified were 2 to 68 ppm toluene and 34 to 78 ppm **ethyl acetate. /**It was/ concluded that platelets of workers are affected by exposure to paint solvents.
[Beving H; Scand J Work Environ Health 10 (4): 229-34 (1984)]**PEER REVIEWED**

Ethyl acetate vapor is irritating to the eyes and respiratory passages of man at concentrations above 400 ppm. ... Due to its irritating properties, employees will not voluntarily remain in such high concentrations. ... This substance is a defatting agent, and prolonged exposure may cause irritation of the skin. Painful conjunctival irritation may occur from splashes in the eye. No chronic systemic effects have been reported in humans.
[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) PublicationNo. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981. 1]**PEER REVIEWED**

Overexposure to **ethyl acetate** may cause irritation of the eyes, nose, & throat. Severe overexposure may cause weakness, drowsiness, & unconsciousness.
[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) PublicationNo. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981.]**PEER REVIEWED**

Humans exposed to a concn of 400 ppm in 1.4 mg/l **ethyl acetate** for a short time were effected by nose and throat irritation. /From table/
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 2981]**PEER REVIEWED**

... **Ethyl acetate** is an irritant of the conjuctiva and mucous membrane of the respiratory tract. Animal experiments have shown that, at very high concentrations, the ester has /CNS depressant/ and lethal effects; at concentrations of 20000 to 43000 ppm, there may be pulmonary edema with hemorrhages, symptoms of central nervous system depression, secondary anemia and damage of the liver. In man, concentrations of 400 ppm cause irritation of the nose and pharynx; cases have also been known of irritation of the conjunctiva with temporary opacity of the cornea. In rare cases exposure may cause sensitization of the mucous membrane and eruptions of the skin. The irritant effect of **ethyl acetate** is less strong than that of propyl acetate or butyl acetate.
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 782]**PEER REVIEWED**

Skin, Eye and Respiratory Irritations:

Irritating to mucous surfaces, particularly the eyes, gums and respiratory passages ... . On repeated or prolonged exposures, it causes conjunctival irritation and corneal clouding.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1514]**PEER REVIEWED**

Medical Surveillance:

Consider the points of attack /eyes, skin, respiratory system/ in placement and periodic examinations.
[Sittig, M. Handbook of Toxic and Hazardous Chemicals and Carcinogens, 1985. 2nd ed. Park Ridge, NJ: Noyes Data Corporation, 1985. 408]**PEER REVIEWED**

Whole Blood: Reference Ranges: Normal - Not established; Exposed - Not established; Toxic - Not stablished.
[Ryan, R.P., C.E. Terry (eds.). Toxicology Desk Reference 4th ed. Volumes 1-3. Taylor & Francis, washington, D.C. 1997. 1256]**PEER REVIEWED**

Serum or Plasma: Reference Ranges: Normal - Not established; Exposed - Not established; Toxic - Not stablished.
[Ryan, R.P., C.E. Terry (eds.). Toxicology Desk Reference 4th ed. Volumes 1-3. Taylor & Francis, washington, D.C. 1997. 1256]**PEER REVIEWED**

Urine: Reference Ranges: Normal - Not established; Exposed - Not established; Toxic - Not stablished.
[Ryan, R.P., C.E. Terry (eds.). Toxicology Desk Reference 4th ed. Volumes 1-3. Taylor & Francis, washington, D.C. 1997. 1256]**PEER REVIEWED**

Respiratory Symptom Questionnaires: Questionnaires have been published by the American Thoracic Society and the British Medical Research Council. These questionnaires have been found to be useful in identification of people with chronic bronchitis, however certain pulmonary function tests such as FEV 1 have been found to be better predictors of chronic airflow obstruction.
[Ryan, R.P., C.E. Terry (eds.). Toxicology Desk Reference 4th ed. Volumes 1-3. Taylor & Francis, washington, D.C. 1997. 1257]**PEER REVIEWED**

Chest Radiography: This test is widely used for assessing pulmonary disease. Chest radiographs have been found to be useful for detection of early lung cancer in asymptomatic people, especially for detection of peripheral tumors such as adenocarcinomas. However, even though OSHA mandates this test for exposure to some toxicants such as asbestos, there are conflicting views on its efficacy in detection of pulmonary disease.
[Ryan, R.P., C.E. Terry (eds.). Toxicology Desk Reference 4th ed. Volumes 1-3. Taylor & Francis, washington, D.C. 1997. 1257]**PEER REVIEWED**

Pulmonary Function Tests: The tests that have been found to be practical for population monitoring include: Spirometry and expiratory flow-volume curves; Determination of lung volumes; Diffusing

capacity for carbon monoxide; Single-breath nitrogen washout; Inhalation challenge tests; Serial measurements of peak expiratory flow; Exercise testing.
[Ryan, R.P., C.E. Terry (eds.). Toxicology Desk Reference 4th ed. Volumes 1-3. Taylor & Francis, washington, D.C. 1997. 1257]**PEER REVIEWED**

Sputum Cytology: Sputum cytology along with chest radiographs have been the standard procedures for detecting early lung cancer in asymptomatic patients. Sputum cytology has been found to be useful for detection of central tumors, especially squamous carcinomas. For this test to be effective, exfoliated respiratory mucosal cells must be present in the expectorated specimen. Pooling of sputum collected over 2-3 days may enhance the sensitivity of this test by increasing the yield of exfoliated cells in the specimen.
[Ryan, R.P., C.E. Terry (eds.). Toxicology Desk Reference 4th ed. Volumes 1-3. Taylor & Francis, washington, D.C. 1997. 1257]**PEER REVIEWED**

Evaluation of Peripheral Neuropathy: Nerve conduction study; Electromyography; Quantitative sensory testing; Thermography.
[Ryan, R.P., C.E. Terry (eds.). Toxicology Desk Reference 4th ed. Volumes 1-3. Taylor & Francis, washington, D.C. 1997. 1258]**PEER REVIEWED**

Evaluation of Central Nervous System Effects: Evaluation of CNS effects can be performed through neuropsychological assessment, which consists of a clinical interview and administration of standardized personality and neuropsychological tests. The areas that the neuropsychology test batteries focus on include the domains of memory and attention; visuoperceptual, visual scanning, visuospatial, and visual memory; and motor speed and reaction time. There is limited data on which components of the test batteries are best indicators of early CNS effects.
[Ryan, R.P., C.E. Terry (eds.). Toxicology Desk Reference 4th ed. Volumes 1-3. Taylor & Francis, washington, D.C. 1997. 1258]**PEER REVIEWED**

Evaluation of Cranial Neuropathies: Evaluation of cranial nerve damage, as evidenced by symptoms such as loss of balance, visual function, smell, taste, or sensation on the face, can be accomplished through a physical examination focusing on tests such as: Smell assessment - standardized odor threshold and identification testing; Vision assessment - standard acuity tests, visual field tests, contrast sensitivity, and color vision measurements (vision assessment); Facial and Trigeminal Nerve assessment - blink reflex (pontogram); Vestibular assessment - pure tone audiometry for bone- and air-conducted sounds, threshold decay at 4 kHz, speech discrimination and speech reception thresholds, tympanograms and acoustic thresholds, electronystagmograms; Hearing assessment - audiometry testing.
[Ryan, R.P., C.E. Terry (eds.). Toxicology Desk Reference 4th ed. Volumes 1-3. Taylor & Francis, washington, D.C. 1997. 1258]**PEER REVIEWED**

Populations at Special Risk:

Employees /with chronic respiratory, skin, liver, or kidney disase may be/ at increased risk from **ethyl acetate.**

[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) PublicationNo. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981. 1]**PEER REVIEWED**

Probable Routes of Human Exposure:

NIOSH (NOES Survey 1981-1983) has statistically estimated that 375,906 workers (87,691 of these are female) are potentially exposed to **ethyl acetate** in the US(1). Occupational exposure to **ethyl acetate** may occur through inhalation and dermal contact with this compound at workplaces where **ethyl acetate** is produced or used(SRC). **Ethyl acetate** was identified (relative abundance) in air samples collected where printing pastes (66%) and paints (30%) were used, in car repair shops (45%), and in various other industries (57%) in Belgium(2). Mean concentrations of **ethyl acetate** in air during parquet work in Finland were 119 ppm during installation with resin adhesives; 319 ppm during puttying; 72 ppm during sanding after puttying; 413 ppm during undercoat varnishing (nitrocellulose); 64 ppm during urea-formaldehyde varnishing; and 1 ppm during work with water-based varnishes(3). It was also detected in air during the use of contact adhesives at mean concentrations of 14 ppm during repair of a textile carpet (dispersion and contact adhesives); 83 ppm during repair of a textile carpet (contact adhesives only); 29 ppm during beading of textile carpets (contact adhesives only); and 71 ppm during repair of bathroom floor mats (dispersion and contact adhesives)(3). **Ethyl acetate** was detected in 36% of all air samples, at a mean concentration of 11 ppm, collected from Finnish furniture factories from 1975 to 1984(4). Breathing zone samples collected during spray painting contained **ethyl acetate** at a geometric mean concentration of 9.51 ppm(5). It was detected in the air of one auto paint shop at a concentration of 10.5 mg/cu m(6). **Ethyl acetate** was identified in 12% of 275 products (including thinners, degreasers, paints, inks, and dome reagents) used in workplaces in various industries(7). **Ethyl acetate** was identified in the breathing zone of shoe factory workers(8). **Ethyl acetate** was detected in the ambient air of shoe factory in Italy in Nov 1991 at median concentrations of 10 and 7 mg/cu m(9). [(1) NIOSH; National Occupational Exposure Survey (NOES) (1983) (2) Veulemans H et al; Am Indust Hyg Assoc J 48: 671-7 (1987) (3) Riala REE, Riihimaki HA; Appl Occup Environ Hyg 6: 301-8 (1991) (4) Priha E; Ann Occup Hyg 30: 289-94 (1986) (5) Myer HE et al; Am Ind Hyg Assoc J 54: 663-70 (1993) (6) Medinilla J, Espigares M; Ann Occup Hyg 32: 509-13 (1988) (7) Lehman E et al; pp. 31-41 in Safety and Health ASP Org Sol Expos Finland April 1985, Riihimaki V, Ulfvarson U, eds NY,NY: Alan R Liss Inc (1986) (8) Ahonen I, Schimberg RW; Br J Ind Med 45: 133-6 (1988) (9) Mutti A et al; Int Arch Occup Environ Health 65: S171-6 (1993)]**PEER REVIEWED**

The general population may be exposed to **ethyl acetate** via inhalation of ambient air, ingestion of food and drinking water, and dermal contact with consumer products containing **ethyl acetate. (**SRC) **PEER REVIEWED**

Body Burden:

Mother's milk from 4 urban areas in the USA, 1 of 8 samples positive(1). 7 out of 12 breath samples collected from nine volunteers in Bayonne and Elizabeth, NJ between July and Dec 1980 contained **ethyl acetate** at unreported concentrations(2). **Ethyl acetate** was identified as a component in 13.7% of

expired air samples from 54 volunteers in the Chicago area at a geometric mean concentration of 0.447 ng/l(3). **Ethyl acetate** was detected in expired air samples from 5 of 8 male volunteers at levels ranging from 0.30 to 190.0 ug/hr(4).
[(1) Pellizzari ED et al; Environ Sci Technol 16: 781-5 (1982) (2) Wallace LA et al; Environ Res 35: 293-319 (1984) (3) Krotoszynski BK et al; J Anal Toxicol 3: 225-34 (1979) (4) Conkle JP et al; Arch Environ Health 30: 290-5 (1975)]**PEER REVIEWED**

Emergency Medical Treatment:

Emergency Medical Treatment:

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The following Overview, *** **ETHYL ACETATE ***,** is relevant for this HSDB record chemical.

Life Support:

- This overview assumes that basic life support measures have been instituted.

Clinical Effects:

SUMMARY OF EXPOSURE

0.2.1.1 ACUTE EXPOSURE

- **Ethyl acetate** is low in toxicity. It is a mild mucous membrane irritant, but is not caustic. In high concentrations it may be a CNS depressant. Animal studies have demonstrated pulmonary edema, decreased cardiac contractility, seizures and hepatic damage, but these have NOT been reported in humans.

0.2.1.2 CHRONIC EXPOSURE

- Chronic poisoning has been described as producing anemia, leucocytosis (transient increase in the white blood cell count) and cloudy swelling, and fatty degeneration of the viscera in animal studies (Sax & Lewis, 1989).

HEENT

0.2.4.1 ACUTE EXPOSURE

- **Ethyl acetate** is irritating to the conjunctivae but leaves no residual effects. Nose and throat irritation is seen at levels greater than 400 ppm for 3 to 5

minutes.

NEUROLOGIC

0.2.7.1 ACUTE EXPOSURE

- Chronic exposure to solvent mixtures including **ethyl acetate** has been associated with poorer performance on neurobehavioral tests. High concentrations orally administered to rabbits caused lack of coordination. High concentrations have intoxicating properties in animals and would be expected to cause narcosis in humans.

DERMATOLOGIC

0.2.14.1 ACUTE EXPOSURE

- Drying as well as skin defatting and cracking may be seen with dermal application. Sensitizations to **ethyl acetate** have been reported but are rare.

Laboratory:

- Various techniques are available, primarily using gas chromatography or spectrometric techniques. Toxic levels have not been established.

Treatment Overview:

SUMMARY EXPOSURE

- Because of rapid hydrolysis and low toxicity, inhalation or ingestion of ethyl acetates seldom requires treatment. Patients should be monitored for CNS depression if large amounts have been ingested.

ORAL EXPOSURE

- Emesis or activated charcoal is unlikely to be necessary due to the low toxicity of these compounds.
- No specific antidotes or treatments are available. Monitor patients ingesting large amounts for CNS depression, respiratory depression, and decreased cardiac contractility.

INHALATION EXPOSURE

- DECONTAMINATION: Move patient to fresh air. Monitor for respiratory distress. If cough or difficulty in breathing develops, evaluate for respiratory tract irritation, bronchitis, or pneumonitis. Administer 100 percent humidified supplemental oxygen with assisted ventilation as required.

EYE EXPOSURE

- DECONTAMINATION: Exposed eyes should be irrigated with copious amounts of tepid water for at least 15 minutes. If irritation, pain, swelling, lacrimation, or

photophobia persist, the patient should be seen in a health care facility.

DERMAL EXPOSURE

- DECONTAMINATION: Wash exposed area extremely thoroughly with soap and water. A physician may need to examine the area if irritation or pain persists.

Range of Toxicity:

- No adverse symptoms were noted in workers exposed to 375 to 1,500 ppm for several months. Humans find concentrations greater than 200 ppm objectionable because of the strong odor. 400 ppm caused nose and throat irritation. The TLV is 400 ppm (1,400 mg/m(3)).

[Rumack BH: POISINDEX(R) Information System. Micromedex, Inc., Englewood, CO, 2001; CCIS Volume 107, edition exp February, 2001. Hall AH & Rumack BH (Eds):TOMES(R) Information System. Micromedex, Inc., Englewood, CO, 2001; CCIS Volume 107, edition exp February, 2001.] **PEER REVIEWED**

Antidote and Emergency Treatment:

For basic treatment: Establish a patent airway. Suction if necessary. Watch for signs of respiratory insufficiency and assist ventilations if necessary. Administer oxygen by nonrebreather mask at 10 to 15 L/min. Monitor for pulmonary edema and treat if necessary ... . Monitor for shock and treat if necessary ... . For eye contamination, flush eyes immediately with water. Irrigate each eye continuously with normal saline during transport ... . Do not use emetics. For ingestion, administer activated charcoal ... . /Esters and related compounds/

[Bronstein, A.C., P.L. Currance; Emergency Care for Hazardous Materials Exposure. 2nd ed. St. Louis, MO. Mosby Lifeline. 1994. 221]**PEER REVIEWED**

For advanced treatment: Consider orotracheal or nasotracheal intubation for airway control in the patient who is unconscious. Positive-pressure ventilation techniques with a bag-valve-mask device may be beneficial. Monitor cardiac rhythm and treat arrhythmias if necessary ... . Start an IV with D5W TKO /SRP: To keep open, "minimal flow rate"/. Ringer's if signs of hypovolemia are present. Watch for signs of fluid overload. For hypotension with signs of hypovolemia, administer fluid cautiously. Consider vasopressors if patient is hypotensive with a normal fluid volume. Watch for signs of fluid overload ... . Consider drug therapy for pulmonary edema ... . Use proparacaine hydrochloride to assist eye irrigation ... . /Esters and related compounds/

[Bronstein, A.C., P.L. Currance; Emergency Care for Hazardous Materials Exposure. 2nd ed. St. Louis, MO. Mosby Lifeline. 1994.,p. 221-2]**PEER REVIEWED**

Animal Toxicity Studies:

Non-Human Toxicity Excerpts:

ANIMAL EXPERIMENTS HAVE SHOWN THAT, IN VERY HIGH CONCN, THE ESTER HAS ... /SRP: CNS DEPRESSANT/ & LETHAL EFFECTS.
[International Labour Office. Encyclopedia of Occupational Health and Safety. Volumes I and II. New York: McGraw-Hill Book Co., 1971. 477]**PEER REVIEWED**

... ANIMALS COULD WITHSTAND CONCN OF **ETHYL ACETATE** OF 2000 PPM FOR 65, 4 HR EXPOSURES WITHOUT APPARENT ILL EFFECTS AS MEASURED BY LACK OF CHANGE IN BODY WT & IN RED & WHITE BLOOD COUNTS.
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Volumes I,II, III. Cincinnati, OH: ACGIH, 1991. 569]**PEER REVIEWED**

CHRONIC, REPEATED INHALATION BY MICE 6 HR/DAY FOR 7 DAYS OF 4200-4400 PPM /& BY GUINEA PIGS OF 2000 PPM/ WAS FOUND ... TO CAUSE NO DEFINITE ... /SRP: CNS DEPRESSANT/ SYMPTOMS, BUT ... NOTED INCR IN ERYTHROCYTES WITH NO CORRESPONDING INCR IN HEMOGLOBIN, & SOME INCR IN POLYMORPHS. ... THERE WAS LOSS OF APPETITE ... NO CHANGE IN ... URINE ... .
[Snyder, R. (ed.). Ethel Browning's Toxicity and Metabolism of Industrial Solvents. Second Edition. Volume 3 Alcohols and Esters. New York, NY: Elsevier, 1992. 239]**PEER REVIEWED**

... SALIVATION, COUGHING, ... PAIN, & FOLLOWED BY DEATH OF 25% OF ANIMALS DURING PERIOD OF DEEP /SRP: CNS DEPRESSION/ ...
[Snyder, R. (ed.). Ethel Browning's Toxicity and Metabolism of Industrial Solvents. Second Edition. Volume 3 Alcohols and Esters. New York, NY: Elsevier, 1992. 239]**PEER REVIEWED**

... EXPOSURE OF RABBITS TO VAPOR AT CONCN WHICH WOULD BE SCARCELY TOLERABLE TO HUMAN BEINGS CAUSED NO CORNEAL DAMAGE DESPITE EXPOSURE FOR 8 HR A DAY, 5 DAYS A WK, FOR ... UP TO 7 WK. ONLY CONJUNCTIVAE GAVE INDICATIONS OF IRRITATION ... STD TESTING ON RABBIT EYES ... RESULTED IN RATING OF 2 ON SCALE OF 10 /10 MOST SEVERE/ ... .
[Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986. 239]**PEER REVIEWED**

WHEN **ETHYL ACETATE** WAS INJECTED INTO THE YOLK SAC OF FRESH FERTILE CHICKEN EGGS BEFORE INCUBATION IN A DOSE OF 9, 22.5, 45, OR 90 MG/EGG, THE HATCHABILITIES WERE 85, 50, 35, AND 15%, RESPECTIVELY.
[Opdyke, D.L.J. (ed.). Monographs on Fragrance Raw Materials. New York: Pergamon Press, 1979. 341]**PEER REVIEWED**

EXPOSURE OF THE FISH /COMMON INDIAN CATFISH, HETEROPNEUSTES FOSSILUS/ TO 170 PPM OF **ETHYL ACETATE** FOR 3, 6, 12, 48, & 96 HR INDUCED MARKED CHANGES IN CARBOHYDRATE METABOLISM. HEPATIC GLYCOGEN LEVELS DECLINED

SIGNIFICANTLY AT 3, 48, & 96 HR, BUT THERE WAS NO MARKED ALTERATION IN MUSCLE GLYCOGEN CONTENT AT ANY OF THE EXPOSURE PERIODS. HYPERGLYCEMIA OCCURRED AT ALL TIME INTERVALS. BLOOD PYRUVATE LEVELS WERE ELEVATED AT 3, 6, 48, & 96 HR. HYPERLACTICEMIA RESULTED AT 3 & 96 HR, BUT HYPOLACTICEMIA OCCURRED AT 6 & 12 HR. IMPAIRMENT OF CARBOHYDRATE METABOLISM MIGHT BE RESPONSIBLE FOR THE TOXIC ACTION OF **ETHYL ACETATE.**
[GUPTA AB, SRIVASTAVA AK; ECOTOXICOL ENVIRON SAF 6 (2): 166-70 (1982)]**PEER REVIEWED**

Ethyl acetate was negative for mutagenicity in Salmonella typhimurium assays.
[NTP; Fiscal Year 1987 Annual Plan p.70 (1987) NTP-87-001]**PEER REVIEWED**

Toxicity Rating: 3. Relatively innocuous, lying on the borderline between toxicity classes 2 and 3. Mild local irritation and central nervous depression. On a molar basis the simple esters of ethyl alcohol are more toxic than ethanol by 4 to 10-fold. ... Toxicity appears to be due to unhydrolyzed esters and not to ethyl alcohol.
[Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984.,p. II-201]**PEER REVIEWED**

... In animals it has a narcotic effect at concentrations of over 5000 ppm. ... Repeated exposures of rabbits to 4450 ppm for 1 hr daily for 40 days resulted in anemia with leukocytosis, and damage to liver and kidneys. Animals exposed to lethal concentrations died with pulmonary edema and hemorrhage. ...
[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) PublicationNo. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981. 1]**PEER REVIEWED**

Cats exposed to a concn of 12,000 ppm in 43 mg/l for 5 hr were affected by the lowest /SRP: CNS depressant/ concn. Exposures to 20,000 ppm in 72 mg/l for 45 min resulted in deep /SRP: CNS depression/, recovery. Exposures to 43,000 ppm in 155 mg/l for 14-16 min resulted in deep /CNS depression/, death. /From table/
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 2982]**PEER REVIEWED**

Chinese hamsters were exposed to **ethyl acetate ...** known to be a strong inducer of aneuploidy in the yeast Saccaromyces cerevisiae. This solvent yielded negative results in the micronucleus test, whereas the vinca alkaloid vindesine used as a positive control substance proved to act as a spindle poison in mammals in vivo.
[Basler A; Mutat Res 174 (1): 11-3 (1986)]**PEER REVIEWED**

Leucopenia without change in differential or red blood cell counts was observed in rats exposed for 4 hr to increasing air concentration of ... **ethyl acetate. ...** This effect was abolished by adrenalectomy. This solvent caused leucopenia only when exposure reached the irritant level. It is discussed that stress associated with the irritative effect of chemicals can confound specific hematological effects.
[Brondeau MT et al; J Appl Toxicol 10 (2): 83-6 (1990)]**PEER

REVIEWED**

In order to determine the lung disease potential of waterproofing sprays, several components of suspected sprays, as well as a commercial spray, were tested on CD-l-mice. Mice placed in inhalation chambers were exposed to aerosols containing one or more of the suspected components, including N-heptane, **ethyl-acetate,** fluororesin, silicone, and a commercial spray. An intermittent inhalation methods was used to prevent the solvents from causing anesthetic death. Mice were sacrificed 1 hour after the end of exposure. The lungs of both exposed and control mice were isolated and examined microscopically for any changes. The amounts released of the were similar. Mice exposed to the commercial and fluororesin sprays were cyanotic and depressed for 1 hour, while those exposed to the other sprays were cyanotic for only several minutes. In almost all mice exposed to the commercial spray, significant changes relative to the controls included a thickened pulmonary alveolar septa, cellular infiltration, fused and hemorrhaged alveolar walls, and diminished alveoli. Fluororesin particles were found in the alveolar space. Significantly more pronounced pathological changes were discovered in mice exposed to the fluororesin spray, relative to the commercial spray. In mice exposed to the silicone spray, significant differences were observed in alveolar collapse and hemorrhage, compared to the controls. The lungs of mice exposed to the N-heptane, **ethyl-acetate,** and fluororesin free sprays were similar to control lungs. In mice exposed to the silicon resin free spray, significant changes, relative to the commercial spray group, included alveolar collapse, hyperemia, hemorrhage and increased thickness and cellular infiltration of the septum. /It was/ concluded that **ethyl-acetate** and N-heptane contained in waterproofing sprays do not cause pulmonary disorders. Instead, fluororesin is implicated in respiratory disorders caused by such sprays.
[Yamashita M, Tanaka J; J Toxicol, Clin Toxicol 33 (6): 631-7 (1995)]**PEER REVIEWED**

The neurotoxic effects of inhaled amyl-acetate, **ethyl-acetate,** and n-butyl-acetate were investigated in mice. Male CFW-albino-mice were exposed to up to 40,000 ppm amyl-acetate, 2,000 ppm **ethyl-acetate,** or 8,000 ppm n-butyl-acetate for 20 minutes in an exposure chamber. Acute neurotoxic effects were assessed by measuring locomotor activity and functional observational battery. Similar acute behavioral effects on locomotor activity were observed in mice following **ethyl-acetate** and n-butyl-acetate exposure, with amyl-acetate inducing little neurotoxic effect. Exposure to the compounds caused changes in posture, with decreased arousal and rearing; increased central nervous system excitability, as manifested by increased tonic and clonic movements; and increased autonomic effects. Also, decreased mobility and righting reflex, and an elevated reaction to sensory stimuli were observed. Handling induced convulsions were produced in some mice following acute exposure; potency differences were observed. Significant decreases in locomotor activity were seen with exposure to **ethyl-acetate** and n-butyl-acetate at the highest concentrations tested, and minimally effective levels for activity decreasing effects were 2,000 and 8,000 ppm for **ethyl-acetate** and n-butyl-acetate, respectively. Rapid recovery was seen in mice after removal from exposure. /It was/ concluded that acute exposure to acetyl-acetate, n-butyl-acetate, and **ethyl-acetate** produces acute neurobehavioral effects which differ from the effects produced by exposure to alkylbenzenes and halogenated hydrocarbon solvents.
[Bowen SE, Balster RL; Fundam and Appl Toxicol 35 (2): 189-96 (1997)]**PEER REVIEWED**

Non-Human Toxicity Values:

LD50 Rat oral 5.6 g/kg /From table/

[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 2980]**PEER REVIEWED**

LD50 Rabbit oral 4.94 g/kg /From table/
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 2980]**PEER REVIEWED**

LD50 Mouse oral 0.44 g/kg /From table/
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 2980]**PEER REVIEWED**

LD50 Guinea pig sc 3.0 g/kg /From table/
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 2980]**PEER REVIEWED**

LD50 Cat sc 3.0 g/kg /From table/
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 2980]**PEER REVIEWED**

LD50 Rat oral 11.3 ml/kg
[The Merck Index. 10th ed. Rahway, New Jersey: Merck Co., Inc., 1983. 545]**PEER REVIEWED**

LD50 Rabbit oral 4.9 g/kg
[Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984.,p. II-201]**PEER REVIEWED**

LD50 Mouse inhalation 1500 ppm/4hr
[Snyder, R. (ed.). Ethel Browning's Toxicity and Metabolism of Industrial Solvents. Second Edition. Volume 3 Alcohols and Esters. New York, NY: Elsevier, 1992. 280]**PEER REVIEWED**

LD50 Rabbit inhalation 2500 ppm/4hr
[Snyder, R. (ed.). Ethel Browning's Toxicity and Metabolism of Industrial Solvents. Second Edition. Volume 3 Alcohols and Esters. New York, NY: Elsevier, 1992. 280]**PEER REVIEWED**

LD50 Rat inhalation 4000 ppm/4hr
[Snyder, R. (ed.). Ethel Browning's Toxicity and Metabolism of Industrial Solvents. Second Edition. Volume 3 Alcohols and Esters. New York, NY: Elsevier, 1992. 280]**PEER REVIEWED**

LC50 Rat inhalation 16,000 ppm/6hr

[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Volumes I,II, III. Cincinnati, OH: ACGIH, 1991. 569]**PEER REVIEWED**

Ecotoxicity Values:

LC50 HETEROPNEUSTES FOSSILIS (COMMON INDIAN CATFISH) 212.5 PPM/96 HR /CONDITIONS OF BIOASSAY NOT SPECIFIED/
[GUPTA AB, SRIVASTAVA AK; ECOTOXICOL ENVIRON SAF 6 (2): 166-70 (1982)]**PEER REVIEWED**

LC50 Pimephales promelas (fathead minnow) 230 mg/l/96 hr (confidence limit 220-250 mg/l). Contamination of chemical in the control tanks - possibly due to volatility of the cmpd. /Conditions of bioassay not specified/
[Brooke, L.T., D.J. Call, D.T. Geiger and C.E. Northcott (eds.). Acute Toxicities of Organic Chemicals to Fathead Minnows (Pimephales Promelas). Superior, WI: Center for LakeSuperior Environmental Studies Univ. of Wisconsin Superior, 1984. 103]**PEER REVIEWED**

EC50 Pimephales promelas (fathead minnow) 220 mg/l/96 hr (confidence limit 210-240 mg/l). Contamination of chemical in the control tanks - possibly due to volatility of the cmpd. Affected fish lost equilibrium prior to death. /Conditions of bioassay not specified/
[Brooke, L.T., D.J. Call, D.T. Geiger and C.E. Northcott (eds.). Acute Toxicities of Organic Chemicals to Fathead Minnows (Pimephales Promelas). Superior, WI: Center for LakeSuperior Environmental Studies Univ. of Wisconsin Superior, 1984. 103]**PEER REVIEWED**

Metabolism/Pharmacokinetics:

Metabolism/Metabolites:

... **ETHYL ACETATE ...** METABOLISM PRODUCES CORRESPONDING ETHYL ALCOHOL & IS PARTLY EXCRETED IN EXHALED AIR & URINE & PARTLY METABOLIZED.
[Snyder, R. (ed.). Ethel Browning's Toxicity and Metabolism of Industrial Solvents. Second Edition. Volume 3 Alcohols and Esters. New York, NY: Elsevier, 1992. 237]**PEER REVIEWED**

AT HIGHER LEVELS, THE RATE OF HYDROLYSIS OF **ETHYL ACETATE /**IN RATS/ APPEARED TO EXCEED ETHANOL OXIDATION, LEADING TO ITS (ETHANOL'S) ACCUMULATION IN THE VASCULAR SYSTEM. ALSO, WHEN IT (**ETHYL ACETATE)** WAS INJECTED IP AT 1.6 G/KG, HYDROLYSIS TO ACETIC ACID AND ETHANOL OCCURRED RAPIDLY.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994.,p. 2983-4]**PEER REVIEWED**

Absorption, Distribution & Excretion:

Ethyl acetate may cause adverse health effects following exposure via inhalation, ingestion or dermal contact. The primary route of absorption responsible for the toxicity of **ethyl acetate** is inhalation.
[Ryan, R.P., C.E. Terry (eds.). Toxicology Desk Reference 4th ed. Volumes 1-3. Taylor & Francis, washington, D.C. 1997. 1253]**PEER REVIEWED**

Biological Half-Life:

... THE BIOLOGICAL HALF-LIFE VALUES OF THE CONVERSION /OF **ETHYL ACETATE** TO ETHANOL/ IN VITRO AND IN VIVO WERE FOUND TO BE 65 AND 5-10 MIN RESPECTIVELY.
[The Chemical Society. Foreign Compound Metabolism in Mammals. Volume 4: A Review of the Literature Published during 1974 and 1975. London: The Chemical Society, 1977. 233]**PEER REVIEWED**

Interactions:

ETHYL ACETATE IN COMBINATION WITH TOLUENE APPEARED TO PRODUCE A MIXTURE OF LOWER TOXICITY THAN THAT OF EITHER COMPOUND ALONE. MIXING OF **ETHYL ACETATE** WITH PROPYLENE OXIDE, PROPYLENE GLYCOL, OR FORMALIN APPEARS TO DECR ITS LD50 VALUE, BUT ITS TOXICITY INCREASES IN COMBINATION WITH MORPHOLINE, ETHYLENE GLYCOL, OR ETHYL ALCOHOL.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 2984]**PEER REVIEWED**

Pharmacology:

Therapeutic Uses:

Anti-Arrhythmia Agents
[National Library of Medicine's Medical Subject Headings online file (MeSH, 1999)]**QC REVIEWED**

... IT HAS BEEN USED INTERNALLY IN A DOSE OF 1 TO 2 CC AS CARMINATIVE & ANTISPASMODIC, ALSO EXTERNALLY AS COUNTERIRRITANT ... .
[Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986. 412]**PEER REVIEWED**

Interactions:

ETHYL ACETATE IN COMBINATION WITH TOLUENE APPEARED TO PRODUCE A MIXTURE OF LOWER TOXICITY THAN THAT OF EITHER COMPOUND ALONE. MIXING OF **ETHYL ACETATE** WITH PROPYLENE OXIDE, PROPYLENE GLYCOL, OR FORMALIN APPEARS TO DECR ITS LD50 VALUE, BUT ITS TOXICITY INCREASES IN COMBINATION WITH MORPHOLINE, ETHYLENE GLYCOL, OR ETHYL ALCOHOL.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New

York, NY: John Wiley & Sons Inc., 1993-1994. 2984]**PEER REVIEWED**

Environmental Fate & Exposure:

Environmental Fate/Exposure Summary:

Ethyl acetate's production and use as a pharmaceutic aid, in artificial fruit essences, and as a solvent may result in its release to the environment through various waste streams. If released to air, a vapor pressure of 93 mm Hg at 25 deg C indicates **ethyl acetate** will exist solely as a vapor in the ambient atmosphere. Vapor-phase **ethyl acetate** will be degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals; the half-life for this reaction in air is estimated to be 9.4 days. If released to soil, **ethyl acetate** is expected to have high mobility based upon an estimated Koc of 59. Volatilization from moist soil surfaces is expected to occur based upon a Henry's Law constant of 1.34X10-4 atm-cu m/mole. **Ethyl acetate's** vapor pressure indicates the potential for volatilization from dry soil surfaces exists. Biodegradation is expected to be an important process in both soil and water, based upon **ethyl acetate's** biodegradation in aqueous screening studies. 93% biodegradation was observed in a complete mix continuous-flow activated sludge system. 26.6 and 57.1% of **ethyl acetate'**s theoretical BOD was reached in 5 days using the standard dilution method and seawater dilution method, respectively. If released into water, **ethyl acetate** is not expected to adsorb to suspended solids and sediment in water based on the estimated Koc. Volatilization from water surfaces is expected to be an important fate process based on **ethyl acetate's** Henry's Law constant. Estimated volatilization half-lives for a model river and model lake are 8.9 hours and 5.6 days, respectively. An estimated BCF of 3.2 suggests the potential for bioconcentration in aquatic organisms is low. **Ethyl acetate's** hydrolysis half-life at 25 deg C and pH 7 is 2.0 years. Occupational exposure to **ethyl acetate** may occur through inhalation and dermal contact with this compound at workplaces where **ethyl acetate** is produced or used or where adhesives, thinners, degreasers, paints, inks, and dome reagents are used. The general population may be exposed to **ethyl acetate** via inhalation of ambient air, ingestion of food and drinking water, or dermal contact with consumer products containing this compound. (SRC)
PEER REVIEWED

Probable Routes of Human Exposure:

NIOSH (NOES Survey 1981-1983) has statistically estimated that 375,906 workers (87,691 of these are female) are potentially exposed to **ethyl acetate** in the US(1). Occupational exposure to **ethyl acetate** may occur through inhalation and dermal contact with this compound at workplaces where **ethyl acetate** is produced or used(SRC). **Ethyl acetate** was identified (relative abundance) in air samples collected where printing pastes (66%) and paints (30%) were used, in car repair shops (45%), and in various other industries (57%) in Belgium(2). Mean concentrations of **ethyl acetate** in air during parquet work in Finland were 119 ppm during installation with resin adhesives; 319 ppm during puttying; 72 ppm during sanding after puttying; 413 ppm during undercoat varnishing (nitrocellulose); 64 ppm during urea-formaldehyde varnishing; and 1 ppm during work with water-based varnishes(3). It was also detected in air during the use of contact adhesives at mean concentrations of 14 ppm during repair of a textile carpet (dispersion and contact adhesives); 83 ppm during repair of a textile carpet (contact adhesives only); 29 ppm during beading of textile carpets (contact adhesives only); and 71 ppm during repair of bathroom floor mats (dispersion and contact adhesives)(3). **Ethyl acetate** was detected in 36% of all air samples, at a mean concentration of 11 ppm, collected from Finnish furniture factories from 1975 to 1984(4). Breathing zone samples collected during spray painting contained **ethyl acetate** at a

geometric mean concentration of 9.51 ppm(5). It was detected in the air of one auto paint shop at a concentration of 10.5 mg/cu m(6). **Ethyl acetate** was identified in 12% of 275 products (including thinners, degreasers, paints, inks, and dome reagents) used in workplaces in various industries(7). **Ethyl acetate** was identified in the breathing zone of shoe factory workers(8). **Ethyl acetate** was detected in the ambient air of shoe factory in Italy in Nov 1991 at median concentrations of 10 and 7 mg/cu m(9).
[(1) NIOSH; National Occupational Exposure Survey (NOES) (1983) (2) Veulemans H et al; Am Indust Hyg Assoc J 48: 671-7 (1987) (3) Riala REE, Riihimaki HA; Appl Occup Environ Hyg 6: 301-8 (1991) (4) Priha E; Ann Occup Hyg 30: 289-94 (1986) (5) Myer HE et al; Am Ind Hyg Assoc J 54: 663-70 (1993) (6) Medinilla J, Espigares M; Ann Occup Hyg 32: 509-13 (1988) (7) Lehman E et al; pp. 31-41 in Safety and Health ASP Org Sol Expos Finland April 1985, Riihimaki V, Ulfvarson U, eds NY,NY: Alan R Liss Inc (1986) (8) Ahonen I, Schimberg RW; Br J Ind Med 45: 133-6 (1988) (9) Mutti A et al; Int Arch Occup Environ Health 65: S171-6 (1993)]**PEER REVIEWED**

The general population may be exposed to **ethyl acetate** via inhalation of ambient air, ingestion of food and drinking water, and dermal contact with consumer products containing **ethyl acetate. (**SRC)
PEER REVIEWED

Body Burden:

Mother's milk from 4 urban areas in the USA, 1 of 8 samples positive(1). 7 out of 12 breath samples collected from nine volunteers in Bayonne and Elizabeth, NJ between July and Dec 1980 contained **ethyl acetate** at unreported concentrations(2). **Ethyl acetate** was identified as a component in 13.7% of expired air samples from 54 volunteers in the Chicago area at a geometric mean concentration of 0.447 ng/l(3). **Ethyl acetate** was detected in expired air samples from 5 of 8 male volunteers at levels ranging from 0.30 to 190.0 ug/hr(4).
[(1) Pellizzari ED et al; Environ Sci Technol 16: 781-5 (1982) (2) Wallace LA et al; Environ Res 35: 293-319 (1984) (3) Krotoszynski BK et al; J Anal Toxicol 3: 225-34 (1979) (4) Conkle JP et al; Arch Environ Health 30: 290-5 (1975)]**PEER REVIEWED**

Natural Pollution Sources:

Ethyl acetate is a natural product of fermentation(1,2). Natural sources of **ethyl acetate** include animal waste, plant volatiles, and microbes(1).
[(1) Graedel TE; Chemical Compounds in the Atmosphere. NY,NY: Academic Press pp. 223-34 (1978) (2) Reed G; Kirk-Othmer Encycl Chem Tech; 3rd ed NY,NY: Wiley Interscience 24: 789 (1983)]**PEER REVIEWED**

Artificial Pollution Sources:

Ethyl acetate's production and use as a pharmaceutic aid (flavor); in artificial fruit essences; as a solvent; in the manufacture of smokeless powder, artificial leather, and photographic films and plates; and in cleaning textiles(1) may result in its release to the environment through various waste streams(SRC).
[(1) Budavari S; The Merck Index - An Encyclopedia of Chemicals,

Drugs, and Biologicals. 12th ed. Whitehouse Station, NJ: Merck and Co Inc p 641 (1996)]**PEER REVIEWED**

Environmental Fate:

TERRESTRIAL FATE: Based on a classification scheme(1), an estimated Koc value of 59(SRC), determined from a log Kow of 0.73(2) and a regression-derived equation(3), indicates that **ethyl acetate** is expected to have high mobility in soil(SRC). Volatilization of **ethyl acetate** from moist soil surfaces is expected to be important(SRC) given a Henry's Law constant of 1.34X10-4 atm-cu m/mole(4). The potential for volatilization of **ethyl acetate** from dry soil surfaces may exist(SRC) based on a vapor pressure of 93 mm Hg(5). **Ethyl acetate** may biodegrade in soil(SRC), based upon its biodegradation in aqueous screening studies(6,7).
[(1) Swann RL et al; Res Rev 85: 23 (1983) (2) Hansch C et al; Exploring QSAR. Hydrophobic, Electronic, and Steric Constants. ACS Professional Reference Book. Heller SR (consult ed) Washington,DC: Amer Chem Soc p. 9 (1995) (3) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington,DC: Amer Chem Soc pp. 4-9 (1990) (4) Butler JAV, Tamchandani CN; J Chem Soc: 952-5 (1935) (5) Daubert TE, Danner RP; Physical and Thermodynamic Properties of Pure Chemicals: Data Compilation. Design Inst Phys Prop Data, Amer Inst Chem Eng., NY,NY: Hemisphere Pub Corp, Vol 2 (1991) (6) Takemoto S et al; Suishitsu Odaka Kenkyu 4: 80-90 (1981) (7) Kincannon DF et al; J Water Pollut Control Fed 55: 157-63 (1983)]**PEER REVIEWED**

AQUATIC FATE: Based on a classification scheme(1), an estimated Koc value of 59(SRC), determined from a log Kow of 0.73(2) and a regression-derived equation(3), indicates that **ethyl acetate** is not expected to adsorb to suspended solids and sediment in water(SRC). **Ethyl acetate** is expected to volatilize from water surfaces(3,SRC) based on a Henry's Law constant of 1.34X10-4 atm-cu m/mole(4). Estimated volatilization half-lives for a model river and model lake are 8.9 hours and 5.6 days, respectively(3,SRC). According to a classification scheme(5), an estimated BCF of 3.2(3,SRC), from the log Kow(2), suggests the potential for bioconcentration in aquatic organisms is low(SRC). Simple esters are resistant to hydrolysis; **ethyl acetate's** hydrolysis half-life at 25 deg C and pH 7 is 2.0 years(6). Biodegradation is expected to be an important process in aquatic systems(SRC), based upon aqueous screening studies(7,8). **Ethyl acetate** reached 26.6 and 57.1% of its theoretical BOD in 5 days using the standard dilution method and seawater dilution method, respectively(7). 99.9% removal of **ethyl acetate** was observed in a complete mix continuous-flow activated sludge system; 93% of this removal was attributed to biodegradation(8). 94% of theoretical methane production was observed after incubation in sediment and groundwater collected from the methanogenic portion of an anoxic aquifer polluted by municipal landfill leachate(9).
[(1) Swann RL et al; Res Rev 85: 23 (1983) (2) Hansch C et al; Exploring QSAR. Hydrophobic, Electronic, and Steric Constants. ACS Professional Reference Book. Heller SR (consult ed) Washington,DC: Amer Chem Soc p 9 (1995) (3) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington,DC: Amer Chem Soc pp. 4-9, 5-4, 5-10, 15-1 to 15-29 (1990) (4) Butler JAV, Tamchandani CN; J Chem Soc: 952-5 (1935) (5) Franke C et al; Chemosphere 29: 1501-14 (1994) (6) Mabey WR et al; J Phys Chem Ref Data Vol 7, No. 2 p. 411 (1978)

(7) Takemoto S et al; Suishitsu Odaka Kenkyu 4: 80-90 (1981) (8) Kincannon DF et al; J Water Pollut Control Fed 55: 157-63 (1983) (9) Sulfita JM, Mormile MR; Environ Sci Technol 27: 976-8 (1993)]**PEER REVIEWED**

ATMOSPHERIC FATE: According to a model of gas/particle partitioning of semivolatile organic compounds in the atmosphere(1), **ethyl acetate,** which has a vapor pressure of 93 mm Hg at 25 deg C(2), is expected to exist solely as a vapor in the ambient atmosphere. Vapor-phase **ethyl acetate** is degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals(SRC); the half-life for this reaction in air is estimated to be 10 days(3,SRC).
[(1) Bidleman TF; Environ Sci Technol 22: 361-367 (1988) (2) Daubert TE, Danner RP; Physical and Thermodynamic Properties of Pure Chemicals: Data Compilation. Design Inst Phys Prop Data, Amer Inst Chem Eng., NY,NY: Hemisphere Pub Corp, Vol 2 (1991) (3) Atkinson R; J Phys Chem Ref Data Monograph 1 p. 166 (1989)]**PEER REVIEWED**

Environmental Biodegradation:

ANAEROBIC: **Ethyl acetate** has been demonstrated to be amenable to anaerobic biodegradation(1). It was mineralized (>75% of theoretical methane production) in 10% sludge from a secondary digester within 8 weeks(2). 96% utilization occurred in an anaerobic reactor with a 20 day retention time(3). **Ethyl acetate,** at a concentration of 1000 mg/l, was readily degraded in batch reactors containing anaerobic solids from an industrial anaerobic digester with some exposure to **ethyl acetate(**4). 100% loss of **ethyl acetate** was observed in aquifer slurries amended with sulfate and nitrate following 244 days and 85 days incubation, respectively(5). 94% of theoretical methane production was observed after incubation in sediment and groundwater collected from the methanogenic portion of an anoxic aquifer polluted by municipal landfill leachate(6).
[(1) Speece RE; Environ Sci Tech 17: 416A-27A (1983) (2) Shelton DR, Tiedje JM; Appl Environ Microbiol 47: 850-7 (1984) (3) Chou WL et al; Biotech Bioeng Symp 8: 391-414 (1979) (4) Schwartz LJ; Appl Biochem Biotehcnol 28/29: 297-305 (1991) (5) Mormile MR et al; Environ Sci Technol 28: 1727-32 (1994) (6) Sulfita JM, Mormile MR; Environ Sci Technol 27: 976-8 (1993)]**PEER REVIEWED**

A review concluded that **ethyl acetate** is easily removed by biological treatment(1). Reported 5 day BOD values using a sewage inoculum range from 36-68% of theoretical(2-5) with the value being somewhat reduced in salt water(2). One investigator reported that **ethyl acetate** was completely degraded in 20 hr using activated sludge(6). In a bench-scale continuous-flow activated sludge reactor with an 8 hour retention time, 99.9% removal (including 17% volatilization loss) was obtained, with 80% of the theoretical BOD(7). **Ethyl acetate** was 90% biooxidized in a 20-day BOD test using a filtered raw sewage seed; it was biooxidized 77% in a 28-day OECD closed-bottle test(8). A screening procedure that was systematically applied to a large number of organic chemicals ranked **ethyl acetate** as being completely biodegraded in a short time by general microorganisms(9). After a 5 hr lag, 43 to 53% of theoretical BOD was obtained in 50 to 70 hr(9). In screening tests, **ethyl acetate,** present at a concentration of 5 ppm, reached 26.6 and 57.1% of its theoretical BOD in 5 days using the standard dilution method and seawater dilution method, respectively(10). 99.9% removal of **ethyl acetate** was observed in a complete mix continuous-flow activated sludge system; 93% of this removal was attributed

to biodegradation(11).
[(1) Thom NS, Agg AR; Proc Roy Soc London B 189: 347-57 (1975) (2) Price KS et al; J Water Pollut Control Fed 46: 63-77 (1974) (3) Ettinger MB; Ind Eng Chem 48: 256-9 (1956) (4) Young RHF et al; J Water Pollut Control Fed 40: 354-68 (1968) (5) Heukelekian H, Rand MC; J Water Pollut Control Assoc 29: 1040-53 (1955) (6) Slave T et al; Rev Chim 25: 666-70 (1974) (7) Stover EL, Kincannon DF; J Water Pollut Control Fed 55: 97-109 (1983) (8) Waggy GT et al; Environ Toxicol Chem 13: 1277-80 (1994) (9) Urano K, Kato Z; J Haz Mat 13: 135-45, 147-59 (1986) (10) Takemoto S et al; Suishitsu Odaka Kenkyu 4: 80-90 (1981) (11) Kincannon DF et al; J Water Pollut Control Fed 55: 157-63 (1983)]**PEER REVIEWED**

Environmental Abiotic Degradation:

The rate constant for the vapor-phase reaction of **ethyl acetate** with photochemically-produced hydroxyl radicals is 1.6X10-12 cu cm/molecule-sec at 25 deg C(1). This corresponds to an atmospheric half-life of about 10 days at an atmospheric concentration of 5X10+5 hydroxyl radicals per cu cm(1,SRC). The observed rate constant for the vapor-phase reaction of **ethyl acetate** with nitrate radicals is 1.4X10-17 cu cm/molecule-sec(2). This corresponds to an atmospheric half-life of about 16 years at an average nighttime nitrate radical concentration of 2X10+8 molecules/cu cm (nitrate radicals are unstable in sunlight)(3,SRC). The rate constant for the reaction of **ethyl acetate** with hydroxyl radicals in aqueous solution is 4.0X10+8 L/mol sec(4). This corresponds to a half-life of about 5.5 years(SRC) at an average aqueous hydroxyl radical concentration of 1X10-17 mol/l(5). Simple esters are resistant to hydrolysis; **ethyl acetate's** hydrolysis half-life at 25 deg C and pH 7 is 2.0 years(6).
[(1) Atkinson R; J Phys Chem Ref Data Monograph 1 p. 166 (1989) (2) Atkinson R; J Phys Chem Ref Data Monograph p. 213 (1994) (3) GEMS; Graphical Exposure Modeling System. FAP. Fate of Atmos Pollut (1986) (4) Buxton GV et al; J Phys Chem Ref Data 17: 513-882 (1988) (5) Mill T et al; Science 207: 886-7 (1980) (6) Mabey WR et al; J Phys Chem Ref Data Vol 7, No. 2 p. 411 (1978)]**PEER REVIEWED**

Environmental Bioconcentration:

An estimated BCF of 3.2 was calculated for **ethyl acetate(**SRC), using a log Kow of 0.73(1) and a regression-derived equation(2). According to a classification scheme(3), this BCF suggests the potential for bioconcentration in aquatic organisms is low(SRC).
[(1) Hansch C et al; Exploring QSAR. Hydrophobic, Electronic, and Steric Constants. ACS Prof Ref Book. Heller SR (consult ed) Washington,DC: Amer Chem Soc p. 9 (1995) (2) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington DC: Amer Chem Soc pp. 5-4, 5-10 (1990) (3) Franke C et al; Chemosphere 29: 1501-14 (1994)]**PEER REVIEWED**

Soil Adsorption/Mobility:

The Koc of **ethyl acetate** is estimated as 59(SRC), using a log Kow of 0.73(1) and a regression-derived equation(2,SRC). According to a classification scheme(3), this estimated Koc value suggests that **ethyl**

acetate is expected to have high mobility in soil(SRC).
[(1) Hansch C et al; Exploring QSAR. Hydrophobic, Electronic, and Steric Constants. ACS Prof Ref Book. Heller SR (consult ed) Washington,DC: Amer Chem Soc p. 9 (1995) (2) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington,DC: Amer Chem Soc pp. 4-9 (1990) (3) Swann RL et al; Res Rev 85: 23 (1983)]**PEER REVIEWED**

Volatilization from Water/Soil:

The Henry's Law constant for **ethyl acetate** is 1.34X10-4 atm-cu m/mole(1). This Henry's Law constant indicates that **ethyl acetate** is expected to volatilize from water surfaces(2,SRC). Based on this Henry's Law constant, the estimated volatilization half-life from a model river (1 m deep, flowing 1 m/sec, wind velocity of 3 m/sec) is estimated as 8.9 hours(2,SRC). The estimated volatilization half-life from a model lake (1 m deep, flowing 0.05 m/sec, wind velocity of 0.5 m/sec) is estimated as 5.6 days(2,SRC). **Ethyl acetate's** Henry's Law constant(1) indicates that volatilization from moist soil surfaces may occur(SRC). The potential for volatilization of **ethyl acetate** from dry soil surfaces may exist(SRC) based on a vapor pressure of 93 mm Hg(3). 7% of the 99.9% removal observed in a continuous flow activated sludge system was attributed to stripping(4).
[(1) Butler JAV, Tamchandani CN; J Chem Soc: 952-5 (1935) (2) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington,DC: Amer Chem Soc pp. 15-1 to 15-29 (1990) (3) Daubert TE, Danner RP; Physical and Thermodynamic Properties of Pure Chemicals: Data Compilation. Design Inst Phys Prop Data, Amer Inst Chem Eng., NY,NY: Hemisphere Pub Corp, Vol 2 (1991) (4) Kincannon DF et al; J Water Pollut Control Fed 55: 157-63 (1983)]**PEER REVIEWED**

Environmental Water Concentrations:

DRINKING WATER: **Ethyl acetate** was detected, not quantified in 3 New Orleans drinking water plants(1). It was detected in drinking water, no levels given(2). **Ethyl acetate** was identified in commercially bottled Artesian water(3).
[(1) Keith LH et al; pp. 329-73 in Identification and Analysis of Organic Pollutants in Water Keith LH ed Ann Arbor Press, Ann Arbor MI (1976) (2) Kool HJ et al; Crit Rev Environ Control 12: 307-57 (1982) (3) Dowty BJ et al; Environ Sci Technol 9: 762-5 (1975)]**PEER REVIEWED**

GROUNDWATER: It was not detected in an aquifer polluted by a paint factory even though **ethyl acetate** was stored in buried tanks that leaked(1).
[(1) Botta D et al; Comm Eur Com Eur 8518 (Anal Org Micropollut Water): 261-75 (1984)]**PEER REVIEWED**

SURFACE WATER: 14 heavily industrialized river basins in USA (204 sites)-only 1 site (Delaware River Basin) positive-1 ppb(1). Hayashida River in Tatsumo City, Japan (site of leather industry) 585 ppb(2). **Ethyl acetate** was identified in water samples from the brook, Rickenbach East, Switzerland, which receives discharges from a paint factory(3).
[(1) Ewing BB et al; Monitoring to Detect Previously Unrecognized

Pollutants in Surface Waters p. 75 USEPA-560/6-77-015 (1977) (2) Yasuhara A et al; Environ Sci Technol 15: 570-3 (1981) (3) Juettner F; Wat Sci Tech 25: 155-64 (1992)]**PEER REVIEWED**

Effluent Concentrations:

Effluent gas from the metal painting factory and from the lumber painting factory contained **ethyl acetate.**
[Yasuhara A et al; Chemosphere 13 (3): 469-82 (1984)]**PEER REVIEWED**

Ethyl acetate was detected, not quantified in oil refinery final effluent(1) and effluent from sewage treatment plants(2). **Ethyl acetate** has been detected in U.S. municipal landfill leachate at concentrations ranging from 42 to 290 g/l(3). **Ethyl acetate** was identified, but not quantified, in hazardous waste samples from a Midwest remedial action site(4). **Ethyl acetate** was detected, but not quantified, in a grab sample of oil refinery final effluent from a refinery in Lockport, IL(5). **Ethyl acetate** was identified as a volatile organic compound in a composite waste sample obtained from a barge which dumped its waste on Feb 9, 1978 at the Puerto Rico dumpsite(6). **Ethyl acetate** was identified in flue gas from a waste incineration plant in Germany(7).
[(1) Ellis DD et al; Arch Environ Contam Toxicol 11: 373-82 (1982) (2) Shackelford WM, Keith LH; Frequency of Organic Compounds Identified in Water USEPA-600/4-76-062 (1976) (3) Roy WR; Contam Groundwaters, Adriano DC et al eds, Sci Rev: Northwood, UK 411-46 (1994) (4) Puskar MA et al; Environ Sci Technol 21: 90-6 (1987) (5) Ellis DD et al; Arch Environ Contam Toxicol 11: 373-82 (1982) (6) Brooks JM et al; Wastes Ocean, Vol 1, Duedall, IW ed, NY,NY: Wiley pp. 171-98 (1983) (7) Jay K, Stieglitz L; Chemosphere 30: 1249-60 (1995)]**PEER REVIEWED**

Atmospheric Concentrations:

URBAN/SUBURBAN: **Ethyl acetate** was detected, not quantified in Leningrad, USSR(1). Average concentrations of **ethyl acetate** in urban air samples collected from four different sites in Stockholm ranged from 0.27 to 2.64 ppb; the average concentration at a site 12 km outside Stockholm was 0.23 ppb(2). It was identified in ambient air from Pasadena, TX, Houston, TX, and Glendora, CA(3). SOURCE AREAS: It was detected in ambient air surrounding Kin Buc waste disposal site (4 sites) 0, trace, 4.1, 230 ug/cu m(4). **Ethyl acetate** was detected in ambient air near a furnace used for incinerating paint wastes at a concentration of 0.7 ppbv(5).
[(1) Ioffe BV et al; J Chromatogr 142: 787-95 (1977) (2) Jonsson AE et al; Environ Int 11: 383-92 (1985) (3) Pellizarri ED; Development of Analytical Techniques for Measuring Ambient Atmospheric Carcinogenic Vapors, EPA-600/2-75-076 (1975) (4) Pellizarri ED; Environ Sci Technol 16: 781-5 (1982) (5) Kelly TJ et al; Environ Sci Technol 27: 1146-53 (1993)]**PEER REVIEWED**

OTHER: 5 out of 8 personal air samples collected from volunteers in Bayonne and Elizabeth, NJ between July and Dec 1980 contained **ethyl acetate** at unreported concentrations(1). **Ethyl acetate** was identified in air at a forest site in the Eggegebirge in North Rhine-Westfalia, West Germany(2). INDOOR: **Ethyl acetate** was detected in air samples taken from preschools in Stockholm(3). **Ethyl acetate** was detected in indoor air samples from Northern Italy at concentrations of 9 and 26 ug/cu m(4).

It was detected in indoor air collected in a machine shop and a new office area at concentrations of 1.4 and 21.8 ppbv, respectively(5). **Ethyl acetate** was detected in the indoor air of 12 out of 12 Canadian homes in Nov and Dec 1986 at concentrations ranging from 3 to 13 ug/cu m, average 8.9 ug/cu m; indoor air concentrations in 6 Canadian homes in Feb and March 1987 ranged from 7 to 494 ug/cu m, average 153 ug/cu m (outdoor air average concentration 10 ug/cu m)(6). **Ethyl acetate** was detected in indoor air of new and recently renovated buildings in Switzerland at a maximum concentration of 1052 ug/cu m(7). It was detected in at least one indoor air sample from 17 locations from two Stockholm preschools(8).
[(1) Wallace LA et al; Environ Res 35: 293-319 (1984) (2) Helmig D et al; Chemosphere 19: 1399-1412 (1989) (3) Noma E et al; Atmos Environ 22: 451-60 (1988) (4) DeBortoli M et al; Environ Int 12: 343-50 (1986) (5) Kelly TJ et al; Environ Sci Technol 27: 1146-53 (1993) (6) Chan CC et al; J Air Waste Manage Assoc 40: 62-7 (1990) (7) Rothweiler H et al; Atmos Environ 26A: 2219-25 (1992) (8) Noma E et al; Aimos Environ 22: 451-60 (1988)]**PEER REVIEWED**

Food Survey Values:

Ethyl acetate forms from the reaction of acetyl coenzyme A with ethanol, and its formation depends greatly on temperature. Maximum formation occurs at 20-25 deg C. Therefore, top fermented beers contain higher amounts of this ester.
[Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984.,p. V24 789 (1984)]**PEER REVIEWED**

Ethyl acetate is found in USA lager beer, 25 to 50 ppm(1). It is a component of Orleans vinegar(2) and artificial grape flavoring(3). **Ethyl acetate** was identified as a volatile component of roasted filberts(4), fried bacon(5), Beaufort cheese(6), blue cheese(7), Idaho Russet Burbank baked potatoes(8), and the edible Korean chamchwi plant(9). Korean salt-fermented anchovy, big-eyed herring, hair tail viscera and shrimp pastes contained **ethyl acetate** at mean concentrations of 3490, 1660, 2340, and 3750 ng/g, respectively(10). **Ethyl acetate** was detected in beer at a concentration of 8 ppm(11). **Ethyl acetate** was identified as a volatile compound in kiwi fruit, comprising 3.9, 4.7, and 1.6% of the components in mature, ripe, and very ripe fruit, respectively(12). It was also identified as a volatile component of pineapple guava at a concentration of 0.11 ug/g(13). Fresh grapefruit juice contained 1.65 ppm **ethyl acetate(**14). **Ethyl acetate** was identified in mature and overripe guava fruits at concentrations of 614.1 and 8884.2 ug/kg, respectively(15). It was identified as a volatile flavor component of the strawberry variety Sivetta and in Golden Delicious apples(16).
[(1) Reed G; Kirk-Othmer Encycl Chem Tech 3rd ed. NY,NY: Wiley Interscience 24: 789 (1983) (2) Webb AD; Kirk-Othmer Encycl Chem Tech 3rd ed. NY,NY: Wiley Interscience 23: 757 (1983) (3) Jones MB; Kirk-Othmer Encycl Chem Tech 3rd ed. NY,NY: Wiley Interscience 4: 712 (1978) (4) Kinlin TE et al; J Agric Food Chem 20: 1021-8 (1972) (5) Ho CT et al; J Agric Food Chem 31: 336-42 (1983) (6) Dumont JP, Adda J; J Agric Food Chem 26: 364-7 (1978) (7) Day EA, Anderson DF; J Agric Food Chem 13: 2-4 (1965) (8) Coleman EC et al; J Agric Food Chem 29: 42-8 (1981) (9) Chung TY et al; J Agric Food Chem 41: 1693-7 (1993) (10) Cha YJ, Cadwallader KR; J Food Sci 60: 19-24 (1995) (11) Hashimoto H, Kuroiwa YJ; J Inst Brewing 72: 151-62 (1966) (12) Bartley JP, Schwede

AM; J Agric Food Chem 37: 1023-5 (1989) (13) Binder RG, Flath RA; J Agric Food Chem 37: 734-6 (1989) (14) Cadwallader KR, Xu Y; J Agric Food Chem 42: 782-4 (1994) (15) Chyau CC et al; J Agric Food Chem 40: 846-9 (1992) (16) Dirinck P et al; Analysis of Volatiles, Berlin,Germany: Walter Degruyter and Co 381-400 (1984)]**PEER REVIEWED**

Ethyl acetate was identified as a volatile component of duck meat, duck fat, Cantonese style roasted duck, and Cantonese style roasted duck gravy at concentrations of <0.05, 2.43, 23.94, and <0.05 ppb wet weight, respectively(1). It was identified as a volatile compound in fried chicken flavor(2), nectarines(3), Concord grape essence(4), three Conn Creek wines(5), Sukiyaki(6), bananas(7), and floured Chickpea seed(8). **Ethyl acetate** was detected in fresh hand-squeezed (mechanically) unpasteurized orange juice from five different cultivars and one hybrid at concentrations of, ppm: 0.28 (0.15 to 0.25) in Valencia oranges; 0.17 to 0.23 (0.15) in Pineapple oranges; 0.12 to 0.13 in Hamlin oranges; 0.77 in Florida navel oranges; 0.17 in California navel oranges; 0.28 in Pera oranges; and 0.12 (0.082) in Ambersweet oranges(9). Large amounts of **ethyl acetate** were detected in headspace from Bisbee Delicious apples at the earliest harvests(10).
[(1) Wu CM, Liou SE; J Agric Food Chem 40: 838-41 (1992) (2) Tang J et al; J Agric Food Chem 31: 1287-92 (1983) (3) Takeoka GR et al; J Agric Food Chem 36: 553-60 (1988) (4) Stevens KL et al; J Food Sci 30: 1006-7 (1965) (5) Shimoda M et al; J Agric Food Chem 41: 1664-66 (1993) (6) Shibamoto T et al; J Agric Food Chem 29: 57-63 (1981) (7) Macku C, Jennings WG; J Agric Food Chem 35: 845-8 (1987) (8) Rembold H et al; J Agric Food Chem 37: 659-62 (1989) (9) Moshonas MG, Shaw PE; J Agric Food Chem 42: 1525-8 (1994) (10) Mattheis JP et al; J Agric Food Chem 39: 1902-6 (1991)]**PEER REVIEWED**

Plant Concentrations:

Ethyl acetate was identified as a volatile component of kiwi fruit flowers(1). Volatile emissions from Scots pine were found to contain **ethyl acetate(**2).
[(1) Tatsuka K et al; J Agric Food Chem 38: 2176-80 (1990) (2) Singh HB, Zimmerman PB; Adv Environ Sci Technol 24: 177-235 (1992)]**PEER REVIEWED**

Fish/Seafood Concentrations:

Ethyl acetate was identified in a sample of mussel collected from the Oarai Coast in Ibaraki, Japan on July 31, 1985 at a concentration of 97.1 ug/g(1).
[(1) Yashuara A, Morita M; Chemosphere 16: 2559-65 (1987)]**PEER REVIEWED**

Milk Concentrations:

Mother's milk from 4 urban areas in the USA, 1 of 8 samples positive(1).
[(1) Pellizarri ED et al; Environ Sci Technol 16: 781-5 (1982)]**PEER REVIEWED**

Other Environmental Concentrations:

Nail polish remover typically contains 40 wt% **ethyl acetate(**1,2). **Ethyl acetate** was identified as a volatile component in fresh and used machine cutting-fluid emulsions at concentrations of 0.171 and 0.310 ug/g, respectively(3). **Ethyl acetate** was identified in the headspace of biodegradable and mixed household waste at concentrations ranging from 0.1 to 1 mg/cu m(4). It was also identified in liquid exudate from garden waste(5). **Ethyl acetate** has been identified as a volatile compound in the headspace of kitchen waste and mold-infested fiber board, kitchen waste exudate, stored food exudate, and garden waste headspace(6). **Ethyl acetate** was identified in 8 printer's inks at concentrations ranging from 0.1 to 13.7% (w/w)(7). **Ethyl acetate** was identified in volatile emissions from Scots pine(8). **Ethyl acetate** comprised 2.0 and 3.7% by weight of total organic gas emissions from industrial surface coatings and thinning solvent, respectively(9). Mean emission rates of **ethyl acetate** from particle board/carpet were 0.025 mg/sq m hr(10). **Ethyl acetate** emissions from whiskey vats averaged 0.593 g/cu m grain input(11). **Ethyl acetate** was found in glue used in Italian shoe factories(12). **Ethyl acetate** was identified as a volatile organic compound present in 3 of 3 samples of poultry manure at concentrations of 10.8, 23.0, and 61.2 mg/kg(13).
[(1) Isacoff H; Kirk-Othmer Encycl Chem Tech; 3rd ed. NY,NY: Wiley Interscience 7: 163 (1979) (2) Wallace LA et al; Res Triangle Inst, Research Triangle Park, NC Report 1991, USEPA/600/D-91/074; (NTIS PB-91-182865) (1991) (3) Yasuhara A et al; Agric Biol Chem 50: 1765-70 (1965) (4) Wilkins K; Chemosphere 29: 47-53 (1994) (5) Wilkins K, Larsen K; Chemosphere 32: 2049-55 (1996) (6) Wilkins CK, Larsen K; J High Resol Chromatogr 18: 373-7 (1995) (7) Rastogi SC; Arch Environ Contam Toxicol 20: 543-7 (1991) (8) Isidorov VA et al; Atmos Environ 19: 1-8 (1985) (9) Harley RA et al; Environ Sci Technol 26: 2395-408 (1992) (10) Colombo A et al; Sci Total Environ 91: 237-49 (1990) (11) Carter RV, Linsky B; Atmos Environ 8: 57-62 (1974) (12) Perbellini L et al; Med Lav 83: 115-19 (1992) (13) Yashuara A; J Chromatogr 387: 371-8 (1987)]**PEER REVIEWED**

Environmental Standards & Regulations:

FIFRA Requirements:

Residues of **ethyl acetate** are exempted from the requirement of a tolerance when used as a solvent or cosolvent in accordance with good agricultural practices as inert (or occasionally active) ingredients in pesticide formulations applied to growing crops or to raw agricultural commodities after harvest.
[40 CFR 180.1001(c) (7/1/97)]**PEER REVIEWED**

As the federal pesticide law FIFRA directs, EPA is conducting a comprehensive review of older pesticides to consider their health and environmental effects and make decisions about their future use. Under this pesticide reregistration program, EPA examines health and safety data for pesticide active ingredients initially registered before November 1, 1984, and determines whether they are eligible for reregistration. In addition, all pesticides must meet the new safety standard of the Food Quality Protection Act of 1996. Pesticides for which EPA had not issued Registration Standards prior to the effective date of FIFRA, as amended in 1988, were divided into three lists based upon their potential for human exposure and other factors, with List B containing pesticides of greater concern and List D pesticides of less concern. **Ethyl acetate** is found on List D. Case No: 4005; Pesticide type: insecticide, herbicide, antimicrobial; Case Status: OPP is reviewing data from the pesticide's producers regarding its

human health and/or environmental effects, or OPP is determining the pesticide's eligibility for reregistration and developing the Reregistration Eligibility Decision (RED) document.; Active ingredient (AI): **Ethyl acetate;** AI Status: The active ingredient is no longer contained in any registered pesticide products ... "cancelled."
[USEPA/OPP; Status of Pesticides in Registration, Reregistration and Special Review p.292 (Spring, 1998) EPA 738-R-98-002]**QC REVIEWED**

TSCA Requirements:

A testing consent order is in effect for **ethyl acetate** for health effects testing. FR citation: 1/23/95.
[40 CFR 799.5000 (7/1/97)]**PEER REVIEWED**

CERCLA Reportable Quantities:

Persons in charge of vessels or facilities are required to notify the National Response Center (NRC) immediately, when there is a release of this designated hazardous substance, in an amount equal to or greater than its reportable quantity of 5000 lb or 2270 kg. The toll free number of the NRC is (800) 424-8802; In the Washington D.C. metropolitan area (202) 426-2675. The rule for determining when notification is required is stated in 40 CFR 302.4 (section IV. D.3.b).
[40 CFR 302.4 (7/1/97)]**PEER REVIEWED**

RCRA Requirements:

U112; As stipulated in 40 CFR 261.33, when **ethyl acetate,** as a commercial chemical product or manufacturing chemical intermediate or an off-specification commercial chemical product or a manufacturing chemical intermediate, becomes a waste, it must be managed according to Federal and/or State hazardous waste regulations. Also defined as a hazardous waste is any residue, contaminated soil, water, or other debris resulting from the cleanup of a spill, into water or on dry land, of this waste. Generators of small quantities of this waste may qualify for partial exclusion from hazardous waste regulations (40 CFR 261.5).
[40 CFR 261.33 (7/1/97)]**PEER REVIEWED**

F003; When **ethyl acetate** is a spent solvent, it is classified as a hazardous waste from a nonspecific source (F003), as stated in 40 CFR 261.31, and must be managed according to State and/or Federal hazardous waste regulations.
[40 CFR 261.31 (7/1/97)]**PEER REVIEWED**

Atmospheric Standards:

This action promulgates standards of performance for equipment leaks of Volatile Organic Compounds (VOC) in the Synthetic Organic Chemical Manufacturing Industry (SOCMI). The intended effect of these standards is to require all newly constructed, modified, and reconstructed SOCMI process units to use the best demonstrated system of continuous emission reduction for equipment leaks of VOC, considering costs, non air quality health and environmental impact and energy requirements. **Ethyl acetate** is produced, as an intermediate or final product, by process units covered under this subpart.
[40 CFR 60.489 (7/1/97)]**PEER REVIEWED**

FDA Requirements:

Certification of this color additive when used as a diluent (in inks for marking fruit & vegetables) is not

necessary for the protection of the public health and therefore batches thereof are exempt from the requirements of section 706(c) of the Federal Food, Drug, and Cosmetic Act. /Restrictions incl no residue./
[21 CFR 73.1 (4/1/97)]**PEER REVIEWED**

Synthetic flavoring substances and adjuvants /for human consumption/ that are generally recognized as safe for their intended use, within the meaning of section 409 of the Act. **Ethyl acetate** is included on this list.
[21 CFR 182.60 (4/1/97)]**PEER REVIEWED**

Synthetic flavoring substances and adjuvants /for animal drugs, feeds, and related products/ that are generally recognized as safe for their intended use, within the meaning of section 409 of the Act. **Ethyl acetate** is included on this list.
[21 CFR 582.60 (4/1/97)]**PEER REVIEWED**

Allowable Tolerances:

Residues of **ethyl acetate** are exempted from the requirement of a tolerance when used as a solvent or cosolvent in accordance with good agricultural practices as inert (or occasionally active) ingredients in pesticide formulations applied to growing crops or to raw agricultural commodities after harvest.
[40 CFR 180.1001(c) (7/1/97)]**PEER REVIEWED**

Chemical/Physical Properties:

Molecular Formula:

C4-H8-O2
[The Merck Index. 10th ed. Rahway, New Jersey: Merck Co., Inc., 1983. 545]**PEER REVIEWED**

Molecular Weight:

88.11
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 641]**PEER REVIEWED**

Color/Form:

CLEAR LIQUID
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 641]**PEER REVIEWED**

Colorless liquid.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 94-116. Washington, D.C.: U.S. Government Printing Office, June 1994. 130]**PEER REVIEWED**

Odor:

CHARACTERISTIC ETHER-LIKE ODOR REMINISCENT OF PINEAPPLE.
[Fenaroli's Handbook of Flavor Ingredients. Volume 2. Edited, translated, and revised by T.E. Furia and N. Bellanca. 2nd ed. Cleveland: The Chemical Rubber Co., 1975. 157]**PEER REVIEWED**

Fragrant odor
[Sax, N.I. Dangerous Properties of Industrial Materials. 6th ed. New York, NY: Van Nostrand Reinhold, 1984. 1315]**PEER REVIEWED**

Ether-like, fruity odor.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 94-116. Washington, D.C.: U.S. Government Printing Office, June 1994. 130]**PEER REVIEWED**

Fruity with a brandy note.
[Gerhartz, W. (exec ed.). Ullmann's Encyclopedia of Industrial Chemistry. 5th ed.Vol A1: Deerfield Beach, FL: VCH Publishers, 1985 to Present.,p. VA11 152]**PEER REVIEWED**

Taste:

PLEASANT TASTE WHEN DILUTED.
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 641]**PEER REVIEWED**

BITTERSWEET, WINE-LIKE BURNING TASTE.
[Fenaroli's Handbook of Flavor Ingredients. Volume 2. Edited, translated, and revised by T.E. Furia and N. Bellanca. 2nd ed. Cleveland: The Chemical Rubber Co., 1975. 157]**PEER REVIEWED**

Ethyl acetate ... contributes a fruity flavor to beer.
[Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984.,p. 24 789 (1984)]**PEER REVIEWED**

Boiling Point:

77 DEG C
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 641]**PEER REVIEWED**

Melting Point:

-83 DEG C
[Weast, R.C. (ed.) Handbook of Chemistry and Physics. 69th ed. Boca Raton, FL: CRC Press Inc., 1988-1989.,p. C-48]**PEER REVIEWED**

Critical Temperature & Pressure:

Critical temperature: 250 DEG C; Critical pressure: 3.8 MN/SQ M
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Density/Specific Gravity:

Sp gr: 0.902 AT 20 DEG C/4 DEG C
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 641]**PEER REVIEWED**

Heat of Combustion:

-5616 CAL/G
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Heat of Vaporization:

87.6 CAL/G
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Octanol/Water Partition Coefficient:

log Kow= 0.73
[Hansch, C., Leo, A., D. Hoekman. Exploring QSAR - Hydrophobic, Electronic, and Steric Constants. Washington, DC: American Chemical Society., 1995. 9]**PEER REVIEWED**

Solubilities:

SOL IN ALCOHOL, ETHER, ACETONE, AND BENZENE
[Weast, R.C. (ed.) Handbook of Chemistry and Physics. 69th ed. Boca Raton, FL: CRC Press Inc., 1988-1989.,p. C-48]**PEER REVIEWED**

MISCIBLE WITH CHLOROFORM
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 641]**PEER REVIEWED**

MISCIBLE IN FIXED & VOLATILE OILS.
[Osol, A. (ed.). Remington's Pharmaceutical Sciences. 16th ed. Easton, Pennsylvania: Mack Publishing Co., 1980. 1232]**PEER REVIEWED**

Very soluble in water (64 g/l at 25 deg C)
[Wasik SP et al; Octanol/Water Partition Coefficients and Aqueous

Solubilities of Organic Compounds p.66 NBS TR81-2406 (1981)]**PEER REVIEWED**

Miscible with oxygenated and chlorinated solvents.
[Ashford, R.D. Ashford's Dictionary of Industrial Chemicals. London, England: Wavelength Publications Ltd., 1994. 387]**PEER REVIEWED**

In water, 8.01X10+4 mg/l at 25 deg C.
[Yalkowsky SH, Dannenfelser RM; Aquasol Database of Aqueous Solubility. Version 5. College of Pharmacy, Univ of Ariz - Tucson, AZ. PC Version (1992)]**PEER REVIEWED**

Spectral Properties:

Index of Refraction = 1.3719 at 20 deg C/D
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 641]**PEER REVIEWED**

MAX ABSORPTION (METHANOL): 209 NM (LOG E= 1.86); SADTLER REFERENCE NUMBER: 4 (IR, PRISM); 3 (IR, GRATING)
[Weast, R.C. (ed.). Handbook of Chemistry and Physics. 60th ed. Boca Raton, Florida: CRC Press Inc., 1979.,p. C-86]**PEER REVIEWED**

IR: 4802 (Coblentz Society Spectral Collection)
[Weast, R.C. and M.J. Astle. CRC Handbook of Data on Organic Compounds. Volumes I and II. Boca Raton, FL: CRC Press Inc. 1985.,p. V1 18]**PEER REVIEWED**

UV: 4-21 (Organic Electronic Spectral Data, Phillips et al, John Wiley & Sons, New York)
[Weast, R.C. and M.J. Astle. CRC Handbook of Data on Organic Compounds. Volumes I and II. Boca Raton, FL: CRC Press Inc. 1985.,p. V1 18]**PEER REVIEWED**

NMR: 79 (Varian Associates NMR Spectra Catalogue)
[Weast, R.C. and M.J. Astle. CRC Handbook of Data on Organic Compounds. Volumes I and II. Boca Raton, FL: CRC Press Inc. 1985.,p. V1 18]**PEER REVIEWED**

MASS: 158 (Atlas of Mass Spectral Data, John Wiley & Sons, New York)
[Weast, R.C. and M.J. Astle. CRC Handbook of Data on Organic Compounds. Volumes I and II. Boca Raton, FL: CRC Press Inc. 1985.,p. V1 18]**PEER REVIEWED**

Intense mass spectral peaks: 43 m/z, 61 m/z, 70 m/z, 73 m/z, 88 m/z
[Pfleger, K., H. Maurer and A. Weber. Mass Spectral and GC Data of Drugs, Poisons and their Metabolites. Parts I and II. Mass Spectra Indexes. Weinheim, FederalRepublic of Germany. 1985. 100]**PEER REVIEWED**

Surface Tension:

24 DYNES/CM AT 20 DEG C
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Vapor Density:

3.04 (AIR= 1)
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 641]**PEER REVIEWED**

Vapor Pressure:

Vapor pressure = 93.2 mm Hg at 25 deg C /from experimentally-derived coefficients/
[Daubert, T.E., R.P. Danner. Physical and Thermodynamic Properties of Pure Chemicals Data Compilation. Washington, D.C.: Taylor and Francis, 1989.]**PEER REVIEWED**

Viscosity:

0.44 CP at 25 deg C
[Weast, R.C. (ed.) Handbook of Chemistry and Physics. 69th ed. Boca Raton, FL: CRC Press Inc., 1988-1989.,p. F-42]**PEER REVIEWED**

Other Chemical/Physical Properties:

ACID VALUE NOT MORE THAN 0.01%
[Fenaroli's Handbook of Flavor Ingredients. Volume 2. Edited, translated, and revised by T.E. Furia and N. Bellanca. 2nd ed. Cleveland: The Chemical Rubber Co., 1975. 157]**PEER REVIEWED**

DISTILLS BETWEEN 76 & 77.5 DEG C
[Osol, A. (ed.). Remington's Pharmaceutical Sciences. 16th ed. Easton, Pennsylvania: Mack Publishing Co., 1980. 1232]**PEER REVIEWED**

DENSITY OF SATURATED AIR (AIR= 1) 1.02; CONVERSION FACTORS: 1 MG/L= 278 PPM; 1 PPM= 3.60 MG/CU M
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 22978]**PEER REVIEWED**

AZEOTROPIC MIXT WITH WATER (6.1% WT/WT), BP: 70.4 DEG C; AZEOTROPIC MIXT WITH WATER (7.8% WT/WT) & ALC (9.0% WT/WT) BP 70.3 DEG; ACQUIRES ACID REACTION WHEN DECOMP BY MOISTURE; ABSORBS WATER (UP TO 3.3% WT/WT)
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 641]**PEER REVIEWED**

LIQUID-WATER INTERFACIAL TENSION: 6.79 DYNES/CM AT 30 DEG C; VAPOR (GAS) SPECIFIC GRAVITY: 3.0; RATIO OF SPECIFIC HEATS OF VAPOR (GAS): 1.080
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Heat of fusion: 28.43 cal/g
[Weast, R.C. (ed.) Handbook of Chemistry and Physics. 69th ed. Boca Raton, FL: CRC Press Inc., 1988-1989.,p. C-667]**PEER REVIEWED**

Heat capacity: 167.4 J/mol K @ 1 atm
[Weast, R.C. (ed.) Handbook of Chemistry and Physics. 69th ed. Boca Raton, FL: CRC Press Inc., 1988-1989.,p. D-174]**PEER REVIEWED**

Henry's Law constant = 1.34X10-4 atm-cu m/mole at 25 deg C
[Butler JAV, Tamchandani CN; J Chem Soc: 952-5 (1935)]**PEER REVIEWED**

More soluble (in water) at lower temps and less sol at higher temps.
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 641]**PEER REVIEWED**

Chemical Safety & Handling:

DOT Emergency Guidelines:

Fire or explosion: Highly flammable: Will be easily ignited by heat, sparks or flames. Vapors may form explosive mixtures with air. Vapors may travel to source of ignition and flash back. Most vapors are heavier than air. They will spread along ground and collect in low confined areas (sewers, basements, tanks). Vapor explosion hazard indoors, outdoors or in sewers. Some may polymerize (P) explosively when heated or involved in a fire. Runoff to sewer may create fire or explosion hazard. Containers may explode when heated. Many liquids are lighter than water.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

Health: May cause toxic effects if inhaled or absorbed through skin. Inhalation or contact with material may irritate or burn skin and eyes. Fire will produce irritating, corrosive and/or toxic gases. Vapors may cause dizziness or suffocation. Runoff from fire control or dilution water may cause pollution.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training

(DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

Public safety: Call Emergency Response Telephone Number. ... Isolate spill or leak area immediately for at least 50 to lOO meters (160 to 330 feet) in all directions. Keep unauthorized personnel away. Stay upwind. Keep out of low areas. Ventilate closed spaces before entering.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

Protective clothing: Wear positive pressure self-contained breathing apparatus (SCBA). Structural firefighters' protective clothing will only provide limited protection.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

Evacuation: Large spill: Consider initial downwind evacuation for at least 300 meters (1000 feet). Fire: If tank, rail car or tank truck is involved in a fire, isolate for 800 meters (1/2 mile) in all directions; also, consider initial evacuation for 800 meters (1/2 mile) in all directions.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

Fire: Caution: All these products have a very low flash point: Use of water spray when fighting fire may be inefficient. Small fires: Dry chemical, CO2, water spray or alcohol-resistant foam. ... Large fires: Water spray, fog or alcohol-resistant foam. Do not use straight streams. Move containers from fire area if you can do it without risk. Fire involving tanks or car/trailer loads: Fight fire from maximum distance or use unmanned hose holders or monitor nozzles. Cool containers with flooding quantities of water until well after fire is out. Withdraw immediately in case of rising sound from venting safety devices or discoloration of tank. Always stay away from the ends of tanks. For massive fire, use unmanned hose holders or monitor nozzles; if this is impossible, withdraw from area and let fire burn.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

Spill or leak: Eliminate all ignition sources (no smoking, flares, sparks or flames in immediate area). All

equipment used when handling the product must be grounded. Do not touch or walk through spilled material. Stop leak if you can do it without risk. Prevent entry into waterways, sewers, basements or confined areas. A vapor suppressing foam may be used to reduce vapors. Absorb or cover with dry earth, sand or other non-combustible material and transfer to containers. Use clean non-sparking tools to collect absorbed material. Large spills: Dike far ahead of liquid spill for later disposal. Water spray may reduce vapor; but may not prevent ignition in closed spaces.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

First aid: Move victim to fresh air. Call emergency medical care. Apply artificial respiration if victim is not breathing. Administer oxygen if breathing is difficult. Remove and isolate contaminated clothing and shoes. In case of contact with substance, immediately flush skin or eyes with running water for at least 20 minutes. Wash skin with soap and water. Keep victim warm and quiet. Effects of exposure (inhalation, ingestion or skin contact) to substance may be delayed. Ensure that medical personnel are aware of the material(s) involved, and take precautions to protect themselves.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

Odor Threshold:

DETECTION IN AIR IS 0.006 TO 0.686 MG/L; DETECTION IN WATER IS 5 PPM.
[Clayton, G. D. and F. E. Clayton (eds.). Patty's Industrial Hygiene and Toxicology: Volume 2A, 2B, 2C: Toxicology. 3rd ed. New York: John Wiley Sons, 1981-1982. 2276]**PEER REVIEWED**

Detection in air: 3.6-1.120 mg cu/m
[Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984.,p. V10 460 (1980)]**PEER REVIEWED**

0.0196 mg/cu m (low odor); 665.0 mg/cu m (high odor); 350 mg/cu m (irritating concn)
[Ruth JH; Am Ind Hyg Assoc J 47: A-142-51 (1986)]**PEER REVIEWED**

Skin, Eye and Respiratory Irritations:

Irritating to mucous surfaces, particularly the eyes, gums and respiratory passages ... . On repeated or prolonged exposures, it causes conjunctival irritation and corneal clouding.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1514]**PEER REVIEWED**

Fire Potential:

DANGEROUS WHEN EXPOSED TO HEAT OR FLAME
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1514]**PEER REVIEWED**

NFPA Hazard Classification:

Health: 1. 1= Materials that, on exposure, would cause irritation, but only minor residual injury, including those requiring the use of an approved air-purifying respirator. These materials are only slightly hazardous to health and only breathing protection is needed.
[National Fire Protection Guide. Fire Protection Guide on Hazardous Materials. 10 th ed. Quincy, MA: National Fire Protection Association, 1991.,p. 325M-47]**PEER REVIEWED**

Flammability: 3. 3= Includes Class IB and IC flammable liquids and materials that can be easily ignited under almost all normal temperature conditions. Water may be ineffective in controlling or extinguishing fires in such materials.
[National Fire Protection Guide. Fire Protection Guide on Hazardous Materials. 10 th ed. Quincy, MA: National Fire Protection Association, 1991.,p. 325M-47]**PEER REVIEWED**

Reactivity: 0. 0= Includes materials that are normally stable, even under fire exposure conditions, and that do not react with water. Normal fire fighting procedures may be used.
[National Fire Protection Guide. Fire Protection Guide on Hazardous Materials. 10 th ed. Quincy, MA: National Fire Protection Association, 1991.,p. 325M-47]**PEER REVIEWED**

Flammable Limits:

LOWER 2.2%; UPPER 9%
[American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices. 5th ed. Cincinnati, OH:American Conference of Governmental Industrial Hygienists, 1986. 239]**PEER REVIEWED**

Flash Point:

7.2 DEG C (OPEN CUP)
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 3806]**PEER REVIEWED**

Autoignition Temperature:

800 DEG F
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 3806]**PEER REVIEWED**

Fire Fighting Procedures:

COOL EXPOSED CONTAINERS WITH WATER.
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

/USE/ CARBON DIOXIDE, DRY CHEM, OR ALCOHOL FOAM.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1514]**PEER REVIEWED**

If material on fire or involved in fire: Do not extinguish fire unless flow can be stopped or safely confined. Use water in flooding quantities as fog. Solid streams of water may be ineffective. Apply water from as far a distance as possible. Cool all affected containers with flooding quantities of water. Use "alcohol" foam, dry chemical or carbon dioxide.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 439]**PEER REVIEWED**

Firefighting Hazards:

FLASHBACK ALONG VAPOR TRAIL MAY OCCUR.
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Explosive Limits & Potential:

THE LIQUID ... PRODUCES A VAPOR THAT FORMS EXPLOSIVE MIXTURES WITH AIR AT NORMAL TEMPERATURES.
[International Labour Office. Encyclopedia of Occupational Health and Safety. Volumes I and II. New York: McGraw-Hill Book Co., 1971. 477]**PEER REVIEWED**

Explosive limits mol fraction in air: Upper 0.090, Lower 0.025
[Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984.,p. V21 369 (1983)]**PEER REVIEWED**

Hazardous Reactivities & Incompatibilities:

... CAN REACT VIGOROUSLY WITH CHLOROSULFONIC ACID, ... OLEUM, K-TERT-BUTOXIDE ...Explosive reaction with lithium tetrahydroaluminate.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1514]**PEER REVIEWED**

Incompatible with nitrates, strong oxidizers, strong alkalies, strong acids.
[Sittig, M. Handbook of Toxic and Hazardous Chemicals and Carcinogens,

1985. 2nd ed. Park Ridge, NJ: Noyes Data Corporation, 1985. 408]**PEER REVIEWED**

Nitrates, strong oxidizers, alkalis & acids.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 130]**QC REVIEWED**

Hazardous Decomposition:

When heated to decomposition it emits acrid smoke and irritating fumes.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1514]**PEER REVIEWED**

On storage, it is slowly decomposed by water.
[Snyder, R. (ed.). Ethel Browning's Toxicity and Metabolism of Industrial Solvents. Second Edition. Volume 3 Alcohols and Esters. New York, NY: Elsevier, 1992. 234]**PEER REVIEWED**

Prior History of Accidents:

The wreck of the MV Ariadne, a Panamanian flag container ship, is examined as a case study of a hazardous substance emergency response in a third world country. /The ship/, carrying a cargo of heavy fuel oil, tetraethyl lead, xylene, toluene, methyl isobutyl ketone, butyl acetate, **ethyl acetate,** and acetone was grounded while departing the harbor of Mogadishu, Somalia. The Somalian government requested a team of technical advisors to help respond appropriately to the emergency. The major issues addressed by the advisory team were the need for additional salvage equipment and expertise, the danger of toxic fumes from the fire and explosions aboard the ship, the presence and possible release of tetraethyl lead, possible port blockage by the wreck, recovery of the chemical drums, and the extent of environmental damage caused by the release of oil, pesticides, and tetraethyl lead into the harbor. ...
[Heare SF et al; 1986 Hazard Matl Spill Conf p.12-18 (1986)]**PEER REVIEWED**

Immediately Dangerous to Life or Health:

2000 ppm (Based on 10% of the lower explosive limit for safety considerations even though the relevant toxicological data indicated that irreversible health effects or impairment of escape existed only at higher concentrations.)
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 130]**QC REVIEWED**

Protective Equipment & Clothing:

ORGANIC VAPOR CANISTER OR AIR MASK; GOGGLES OR FACE SHIELD.
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Wear appropriate clothing to prevent repeated or prolonged skin contact.
[Sittig, M. Handbook of Toxic and Hazardous Chemicals and Carcinogens, 1985. 2nd ed. Park Ridge, NJ: Noyes Data Corporation, 1985. 409]**PEER REVIEWED**

Breakthrough times greater than one hour reported by (normally) two or more testers for butyl rubber (Butyl). Some data usually from immersion tests suggesting breakthrough times greater than one hour are not likely for natural rubber (Nat Rub), polyethylene (PE) and polyvinyl alcohol (PVA). Breakthrough times less (usually significantly less) than one hour reported by (normally) two or more testers for neoprene (Neop), nitrile rubber (nitrile), and polyvinyl chloride (PVC). No data for neoprene /styrene-butadiene rubber (Neop/ SBR), nitrile rubber/polyvinyl chloride (Nitrile/PVC), chlorinated polyethylene (CPE), polyurethane (PU), styrene-butadiene rubber (SBR) and viton.
[ACGIH; Guidelines Select of Chem Protect Clothing Volume #1 Field Guide p.44 (1983)]**PEER REVIEWED**

Wear appropriate personal protective clothing to prevent skin contact.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 131]**QC REVIEWED**

Wear appropriate eye protection to prevent eye contact.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 131]**QC REVIEWED**

Recommendations for respirator selection. Max concn for use: 2000 ppm. Respirator Class(es): Any supplied-air respirator operated in a continuous flow mode. Eye protection needed. Any powered, air-purifying respirator with organic vapor cartridge(s). Eye protection needed. Any chemical cartridge respirator with a full facepiece and organic vapor cartridge(s). Any air-purifying, full-facepiece respirator (gas mask) with a chin-style, front- or back-mounted organic vapor canister. Any self-contained breathing apparatus with a full facepiece. Any supplied-air respirator with a full facepiece.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 131]**QC REVIEWED**

Recommendations for respirator selection. Condition: Emergency or planned entry into unknown concn or IDLH conditions: Respirator Class(es): Any self-contained breathing apparatus that has a full facepiece and is operated in a pressure-demand or other positive-pressure mode. Any supplied-air respirator that has a full facepiece and is operated in a pressure-demand or other positive-pressure mode in combination with an auxiliary self-contained breathing apparatus operated in pressure-demand or other positive-pressure mode.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 131]**QC REVIEWED**

Recommendations for respirator selection. Condition: Escape from suddenly occurring respiratory hazards: Respirator Class(es): Any air-purifying, full-facepiece respirator (gas mask) with a chin-style, front- or back-mounted organic vapor canister. Any appropriate escape-type, self-contained breathing

apparatus.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 131]**QC REVIEWED**

Wear positive-pressure SCBA and protective equipment ... . If special chemical protective clothing is required, consult the chemical manufacturer or specific protective clothing compatibility charts. Delay entry until trained personnel and proper protective equipment are available. Remove patient from contaminated area. Quickly remove and isolate patient's clothing, jewelry, and shoes. Gently blot excess liquids with absorbent material. Rinse patient with warm water, 30 deg C/86 deg F, if possible. Wash patient with Tincture of Green Soap or a mild liquid soap and large quantities of water.
[Bronstein, A.C., P.L. Currance; Emergency Care for Hazardous Materials Exposure. 2nd ed. St. Louis, MO. Mosby Lifeline. 1994. 221]**PEER REVIEWED**

SRP: Contaminated protective clothing should be segregated in such a manner so that there is no direct personal contact by personnel who handle, dispose, or clean the clothing. Quality assurance to ascertain the completeness of the cleaning procedures should be implemented before the decontaminated protective clothing is returned for reuse by the workers. Contaminated clothing should not be taken home at end of shift, but should remain at employee's place of work for cleaning.
PEER REVIEWED

Preventive Measures:

USE EFFECTIVE FUME REMOVAL DEVICE /IN LABORATORY/.
[Association of Official Analytical Chemists. Official Methods of Analysis. 10th ed. and supplements. Washington, DC: Association of Official Analytical Chemists, 1965. New editions through13th ed. plus supplements, 1982.,p. 13/882 51.057]**PEER REVIEWED**

Employees should wash promptly when skin is wet or contaminated. Remove clothing immediately if wet or contaminated to avoid flammability hazard.
[Sittig, M. Handbook of Toxic and Hazardous Chemicals and Carcinogens, 1985. 2nd ed. Park Ridge, NJ: Noyes Data Corporation, 1985. 409]**PEER REVIEWED**

Avoid breathing vapors. Keep upwind. Wear appropriate chemical protective gloves, boots and goggles. Do not handle broken packages unless wearing appropriate personal protective equipment. Wash away any material which may have contacted the body with copious amounts of water or soap and water.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 439]**PEER REVIEWED**

Contact lenses should not be worn when working with this chemical.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 131]**QC REVIEWED**

SRP: The scientific literature for the use of contact lenses in industry is conflicting. The benefit or

detrimental effects of wearing contact lenses depend not only upon the substance, but also on factors including the form of the substance, characteristics and duration of the exposure, the uses of other eye protection equipment, and the hygiene of the lenses. However, there may be individual substances whose irritating or corrosive properties are such that the wearing of contact lenses would be harmful to the eye. In those specific cases, contact lenses should not be worn. In any event, the usual eye protection equipment should be worn even when contact lenses are in place.
PEER REVIEWED

If material not on fire and not involved in fire: Keep sparks, flames and other sources of ignition away. Keep material out of water sources and sewers. Build dikes to contain flow as necessary. Attempt to stop leak if without undue personnel hazard. Use water spray to disperse vapors and dilute standing pools of liquid.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 439]**PEER REVIEWED**

SRP: Contaminated protective clothing should be segregated in such a manner so that there is no direct personal contact by personnel who handle, dispose, or clean the clothing. Quality assurance to ascertain the completeness of the cleaning procedures should be implemented before the decontaminated protective clothing is returned for reuse by the workers. Contaminated clothing should not be taken home at end of shift, but should remain at employee's place of work for cleaning.
PEER REVIEWED

The worker should immediately wash the skin when it becomes contaminated.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 131]**QC REVIEWED**

Work clothing that becomes wet should be immediately removed due to its flammability hazard.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 131]**QC REVIEWED**

An analysis of breakthrough times of low boiling organic solvent vapors in a commercial respirator cartridge under steady state and pulsating flow conditions was performed. A KGC-8 respirator cartridge packed with 22.5 grams of activated charcoal was exposed to 0, 100, 300, or 900 ppm carbon-tetrachloride, **ethyl-acetate,** methyl-acetate, acetone, or dichloromethane vapor under steady state or pulsed flow conditions in custom built apparatus. The steady state flow condition was achieved by setting the respirator cartridge in its holder and passing each solvent vapor through it at a flow rate of 30 liter per minute (l/min). The pulsating flow condition was achieved placing the respirator cartridge in a Tedler bag, expanding the bag by introducing each test vapor, and 'inhaling' the test vapor through the respirator cartridge using a breathing machine drawing 1.5 liters air per cycle at the rate 20 cycles/min. The total flow rate was adjusted to be similar to the 301/min rate utilized the steady state flow experiments. Solvent vapor concentrations were measured upstream and downstream from the cartridge by gas chromatography. Breakthrough times were determined as the time required for the solvent vapor concentrations downstream from the cartridge to increase to 5 ppm. The data were analyzed by logistic regression techniques. After converting the data to logarithms, the breakthrough times of all five solvents

were linearly, inversely proportional to their initial concentrations under both steady state and pulsed flow conditions. The slopes of the lines were smaller for the solvents with the lower boiling points. The ratios of the breakthrough times measured under the pulsating flow to the steady slate flow condition (B/A ratio) varied from 0.77 to 0.71 for dichloromethane. The B/A ratios for the lOO ppm initial concentrations of the other four solvents varied only from 0.95 to 1.01. This indicated that except in the case of dichloromethane, there are no large differences in breakthrough tire under the two different flow conditions at lOO ppm. At the other concentrations, in each experiment as the concentration of the test vapor increased the breakthrough times under the pulsating flow condition became shorter compared to the steady state flow condition. /It was/ concluded that breakthrough of low boiling solvent vapors in respirator cartridges occurs earlier under pulsating flow than under steady state conditions.
[Tanaka S et al; Industrial Health 34 (2): 125-31 (1996)]**PEER REVIEWED**

Stability/Shelf Life:

SLOWLY DECOMP BY MOISTURE.
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 3806]**PEER REVIEWED**

Shipment Methods and Regulations:

No person may /transport,/ offer or accept a hazardous material for transportation in commerce unless that person is registered in conformance ... and the hazardous material is properly classed, described, packaged, marked, labeled, and in condition for shipment as required or authorized by ... /the hazardous materials regulations (49 CFR 171-177)./
[49 CFR 171.2 (7/1/96)]**PEER REVIEWED**

The International Air Transport Association (IATA) Dangerous Goods Regulations are published by the IATA Dangerous Goods Board pursuant to IATA Resolutions 618 and 619 and constitute a manual of industry carrier regulations to be followed by all IATA Member airlines when transporting hazardous materials.
[IATA. Dangerous Goods Regulations. 38th ed. Montreal, Canada and Geneva, Switzerland: International Air Transport Association, Dangerous Goods Board, January, 1997. 146]**PEER REVIEWED**

The International Maritime Dangerous Goods Code lays down basic principles for transporting hazardous chemicals. Detailed recommendations for individual substances and a number of recommendations for good practice are included in the classes dealing with such substances. A general index of technical names has also been compiled. This index should always be consulted when attempting to locate the appropriate procedures to be used when shipping any substance or article.
[IMDG; International Maritime Dangerous Goods Code; International Maritime Organization p.3075 (1988)]**PEER REVIEWED**

Storage Conditions:

KEEP TIGHTLY CLOSED IN COOL PLACE & AWAY FROM FIRE.
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc.,

1996. 3806]**PEER REVIEWED**

DURING TRANSPORT: STABLE DURING TRANSPORT. STORAGE TEMPERATURE: AMBIENT. VENTING: OPEN (FLAME ARRESTER) OR PRESSURE-VACUUM.
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

On storage, it is slowly decomposed by water.
[Snyder, R. (ed.). Ethel Browning's Toxicity and Metabolism of Industrial Solvents. Second Edition. Volume 3 Alcohols and Esters. New York, NY: Elsevier, 1992. 234]**PEER REVIEWED**

Cleanup Methods:

1. REMOVE ALL IGNITION SOURCES. 2. VENTILATE AREA OF SPILL OR LEAK. 3. FOR SMALL QUANTITIES, ABSORB ON PAPER TOWELS. EVAPORATE IN A SAFE PLACE (SUCH AS A FUME HOOD). ALLOW SUFFICIENT TIME FOR EVAPORATING VAPORS TO COMPLETELY CLEAR THE HOOD DUCTWORK. BURN THE PAPER IN A SUITABLE LOCATION AWAY FROM COMBUSTIBLE MATERIALS. LARGE QUANTITIES CAN BE COLLECTED AND ATOMIZED IN A SUITABLE COMBUSTION CHAMBER. **ETHYL ACETATE** SHOULD NOT BE ALLOWED TO ENTER A CONFINED SPACE, SUCH AS A SEWER, BECAUSE OF THE POSSIBILITY OF AN EXPLOSION.
[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) PublicationNo. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981. 3]**PEER REVIEWED**

Disposal Methods:

Generators of waste (equal to or greater than 100 kg/mo) containing this contaminant, EPA hazardous waste numbers U112 and F003, must conform with USEPA regulations in storage, transportation, treatment and disposal of waste.
[40 CFR 240-280, 300-306, 702-799 (7/1/89)]**PEER REVIEWED**

Incineration: Burn waste material in an approved waste disposal incinerator.
[United Nations. Treatment and Disposal Methods for Waste Chemicals (IRPTC File). Data Profile Series No. 5. Geneva, Switzerland: United Nations Environmental Programme, Dec. 1985. 72]**PEER REVIEWED**

1. BY ABSORBING IT IN VERMICULITE, DRY SAND, EARTH, OR A SIMILAR MATERIAL. 2. BY ATOMIZING IN A SUITABLE COMBUSTION CHAMBER.
[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) PublicationNo. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981. 3]**PEER REVIEWED**

Ethyl acetate is a waste chemical stream constituent which may be subjected to ultimate disposal by controlled incineration.

[USEPA; Engineering Handbook for Hazardous Waste Incineration p.2-6 (1981) EPA 68-03-3025]**PEER REVIEWED**

A good candidate for rotary kiln incineration at a temperature range of 820 to 1,600 deg C and residence times of seconds for liquids and gases, and hours for solids. A good candidate for liquid injection incineration at a temperature range of 650 to 1,600 deg C and a residence time of 0.1 to 2 seconds. A good candidate for fluidized bed incineration at a temperature range of 450 to 980 deg C and residence times of seconds for liquids and gases, and longer for solids.
[USEPA; Engineering Handbook for Hazardous Waste Incineration p.3-13 (1981) EPA 68-03-3025]**PEER REVIEWED**

The following wastewater treatment technologies have been investigated for **Ethyl acetate:**
Concentration process: Biological treatment.
[USEPA; Management of Hazardous Waste Leachate, EPA Contract No.68-03-2766 p.E-33 (1982)]**PEER REVIEWED**

The following wastewater treatment technologies have been investigated for **Ethyl acetate:**
Concentration process: Activated carbon.
[USEPA; Management of Hazardous Waste Leachate, EPA Contract No.68-03-2766 p.E-133 (1982)]**PEER REVIEWED**

Occupational Exposure Standards:

OSHA Standards:

Permissible Exposure Limit: Table Z-1 8-hr Time Weighted Avg: 400 ppm (1400 mg/cu m).
[29 CFR 1910.1000 (7/1/98)]**QC REVIEWED**

Threshold Limit Values:

8 hr Time Weighted Avg (TWA) 400 ppm
[American Conference of Governmental Industrial Hygienists. Threshold Limit Values (TLVs) for Chemical Substances and Physical Agents Biological Exposure Indices for 1998. Cincinnati, OH: ACGIH, 1998. 36]**QC REVIEWED**

Excursion Limit Recommendation: Excursions in worker exposure levels may exceed three times the TLV-TWA for no more than a total of 30 min during a work day, and under no circumstances should they exceed five times the TLV-TWA, provided that the TLV-TWA is not exceeded.
[American Conference of Governmental Industrial Hygienists. Threshold Limit Values (TLVs) for Chemical Substances and Physical Agents Biological Exposure Indices for 1998. Cincinnati, OH: ACGIH, 1998. 6]**QC REVIEWED**

NIOSH Recommendations:

Recommended Exposure Limit: 10 Hr Time-Weighted Avg: 400 ppm (1400 mg/cu m).
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing

Office, 1997. 130]**QC REVIEWED**

Immediately Dangerous to Life or Health:

2000 ppm (Based on 10% of the lower explosive limit for safety considerations even though the relevant toxicological data indicated that irreversible health effects or impairment of escape existed only at higher concentrations.)
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 130]**QC REVIEWED**

Other Occupational Permissible Levels:

USSR (1973): 55 ppm; Czechoslovakia (1969): 110 ppm; Sweden (1974): 300 ppm; Italy (1975): 220 ppm.
[American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices. 5th ed. Cincinnati, OH:American Conference of Governmental Industrial Hygienists, 1986.]**PEER REVIEWED**

Manufacturing/Use Information:

Major Uses:

The active ingredient is no longer contained in any registered pesticide products ... "cancelled."
[USEPA/OPP; Status of Pesticides in Registration, Reregistration and Special Review p.292 (Spring, 1998) EPA 738-R-98-002]**QC REVIEWED**

ARTIFICIAL FRUIT ESSENCES; SOLVENT FOR NITROCELLULOSE, VARNISHES, LACQUERS, AEROPLANE DOPES; MANUFACTURE OF SMOKELESS POWDER, ARTIFICIAL LEATHER, & PHOTOGRAPHIC FILMS & PLATES, ARTIFICIAL SILK, PERFUMES; CLEANING TEXTILES; PHARMACEUTIC AID (FLAVOR)
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 641]**PEER REVIEWED**

SYNTHETIC FLAVORING; USED IN FOODS
[Fenaroli's Handbook of Flavor Ingredients. Volume 2. Edited, translated, and revised by T.E. Furia and N. Bellanca. 2nd ed. Cleveland: The Chemical Rubber Co., 1975. 157]**PEER REVIEWED**

FOR CONTACT LENS MOLD RELEASE.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 2977]**PEER REVIEWED**

SOLVENT FOR COATINGS (EG, SHELLAC) & PLASTICS (EG, VINYL RESINS); OTHER SOLVENT USES (EG, INKS); CHEM INTERMEDIATE; AROMA ENHANCER IN GRAPE BEVERAGES.

[SRI]**PEER REVIEWED**

Organic synthesis
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 12th ed. New York, NY: Van Nostrand Rheinhold Co., 1993 478]**PEER REVIEWED**

Solvent in production of adhesives, fingernail polishes; extraction solvent in production of pharmaceuticals and foods; carrier solvent for herbicides; component of lacquer thinner.
[CHEMICAL PRODUCTS SYNOPSIS: Ethyl Acetate (1983)]**PEER REVIEWED**

MEDICATION
PEER REVIEWED

/Used/ ... as diluents in inks for marking fruits and vegetables.
[21 CFR 73.1 (4/1/97)]**PEER REVIEWED**

In the manufacture of vaccines, splitting influenza virus.
[Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984.,p. V23 632 (83)]**PEER REVIEWED**

In fruit and brandy flavors.
[Gerhartz, W. (exec ed.). Ullmann's Encyclopedia of Industrial Chemistry. 5th ed.Vol A1: Deerfield Beach, FL: VCH Publishers, 1985 to Present.,p. VA11 152]**PEER REVIEWED**

Manufacturers:

Eastman Chemical Company, Hq, P.O. Box 511, Kingsport, TN 37662, (423) 229-2000; Tennessee Eastman Division, Hq, P.O Box 511, Kingsport, TN 37662, (423) 229-2000; Production site: Kingsport, TN 37662; Texas Eastman Division, Hq, P.O. Box 744, Longview, TX 75607-7444, (903) 237-5000; Production site: Longview, TX 75607
[SRI. 1997 Directory of Chemical Producers - United States of America. Menlo Park, CA: SRI International 1997. 583]**PEER REVIEWED**

Hoechst Celanese Corp, Hq, Route 202-206 North, P.O. Box 2500, Somerville, NJ 08876, (908) 231-2000; Celanese Ltd., Hq, 1601 West LBJ Freeway, Dallas, TX 75381, (972) 277-4000; Chemicals Division; Production site: P.O. Box 937, Pampa, TX 79065
[SRI. 1997 Directory of Chemical Producers - United States of America. Menlo Park, CA: SRI International 1997. 583]**PEER REVIEWED**

Monsanto Company, Hq, 800 North Lindbergh Boulevard, St. Louis, MO 63167, (314) 694-1000; Chemical Group; Production sites: 730 Worcester Street, Springfield, MA 01151 (Indian Orchard Plant); 5100 W. Jefferson, Trenton, MI 48183
[SRI. 1997 Directory of Chemical Producers - United States of America. Menlo Park, CA: SRI International 1997. 583]**PEER REVIEWED**

Methods of Manufacturing:

Co-product of butane oxidation to acetic acid at 175 deg C and 50 atm in the presence of catalytic cobalt and chromium ions; co-product of the ethanolysis of polyvinyl acetate to polyvinyl alcohol.
[CHEMICAL PRODUCTS SYNOPSIS: Ethyl Acetate (1983)]**PEER REVIEWED**

Acetaldehyde (Tishchenko reaction); ethanol + acetic acid (esterification); polyvinyl acetate + ethanol (transesterification; byproduct of polyvinyl alcohol reaction).
[Ashford, R.D. Ashford's Dictionary of Industrial Chemicals. London, England: Wavelength Publications Ltd., 1994. 387]**PEER REVIEWED**

By heating acetic acid and ethyl alcohol in presence of sulfuric acid and distilling.
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 12th ed. New York, NY: Van Nostrand Rheinhold Co., 1993 477]**PEER REVIEWED**

Formulations/Preparations:

GRADES: COMMERCIAL, 85-88%; 95-98%; 99%; NF /NATIONAL FORMULARY GRADE OF CHEMICAL/ (99%); FCC /FOOD CHEMICAL CODEX/.
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 12th ed. New York, NY: Van Nostrand Rheinhold Co., 1993 478]**PEER REVIEWED**

Nail polish remover typically 40 wt% **ethyl acetate.**
[Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984.,p. V7 163]**PEER REVIEWED**

Impurities:

In the 85-88% grade, the major constituent other than **ethyl acetate** is ethanol.
[CHEMICAL PRODUCTS SYNOPSIS: Ethyl Acetate (1983)]**PEER REVIEWED**

Consumption Patterns:

SOLVENT FOR: COATINGS (EG, SHELLAC), 65%; PLASTICS (EG, VINYL RESINS), 12%; OTHER SOLVENT USES (EG, INKS), 20%; CHEM INTERMEDIATE, 3% (1983)
[SRI]**PEER REVIEWED**

Lacquers and enamels, 60%; inks, 15%; miscellaneous, 25% (1983) /estimate/
[CHEMICAL PRODUCTS SYNOPSIS: Ethyl Acetate (1983)]**PEER REVIEWED**

CHEMICAL PROFILE: **Ethyl Acetate.** Coatings solvent, 40%; exports, 38%; miscellaneous solvent uses, 12%; plastics, 8%; chemical synthesis, 2%.
[Kavaler AR; Chemical Marketing Reporter 235 (2): 46 (1989)]**PEER REVIEWED**

CHEMICAL PROFILE: **Ethyl acetate.** Demand: 1988: 210 million lb; 1989: 210 million lb; 1993 /projected/: 220 million lb. (Includes exports, but not imports, which totaled 30 million lb last year.)
[Kavaler AR; Chemical Marketing Reporter 235 (2): 46 (1989)]**PEER REVIEWED**

CHEMICAL PROFILE: **Ethyl Acetate.** Demand, million pounds: 325 in 1996, 335 in 1997, est 400 in 2001 (includes exports of 100 to 125 million pounds; but not imports in the range of 20 million to 30 million pounds annually). Uses: coatings solvent, 60%; process solvent, including pharmaceuticals and organic synthesis, 15%; inks solvent, 15%; miscellaneous solvent uses, including adhesives and cosmetics, 10%.
[Kavaler AR; Chemical Marketing Reporter, Oct 6, 1997 (1997)]**PEER REVIEWED**

U. S. Production:

(1978) 8.26X10+10 G
[SRI]**PEER REVIEWED**

(1982) 1.07X10+11 G
[SRI]**PEER REVIEWED**

(1985) 8.71X10+10 g
[USITC. SYN ORG CHEM-U.S. PROD/SALES p.266 (1985)]**PEER REVIEWED**

(1986) 1.92X10+8 lb
[USITC. SYN ORG CHEM-U.S. PROD/SALES. PRELIMINARY p.C/P-87-5 (1986)]**PEER REVIEWED**

U. S. Imports:

(1978) 2.90X10+9 G
[SRI]**PEER REVIEWED**

(1982) 5.15X10+9 G
[SRI]**PEER REVIEWED**

(1985) 4.40X10+9 g
[BUREAU OF THE CENSUS. U.S. IMPORTS FOR CONSUMPTION AND GENERAL IMPORTS p.1-582 (1985)]**PEER REVIEWED**

(1986) 9.14X10+6 lb
[BUREAU OF THE CENSUS. US IMPORTS FOR CONSUMPTION AND GENERAL IMPORTS P. 1-528 (1986)]**PEER REVIEWED**

U. S. Exports:

(1978) 2.88X10+10 G
[SRI]**PEER REVIEWED**

(1982) 4.99X10+10 G
[SRI]**PEER REVIEWED**

(1985) 3.53X10+10 g
[BUREAU OF THE CENSUS. U.S. EXPORTS, SCHEDULE E, p.2-77 (1985)]**PEER REVIEWED**

(1987) 6.8X10+7 lb
[BUREAU OF THE CENSUS. U. S. EXPORTS, SCHEDULE E, P.2-80 (OCTOBER 1987)]**PEER REVIEWED**

(1988) 3.23X10+6 lb
[BUREAU OF THE CENSUS. U. S. EXPORTS, SCHEDULE E, P.2-59 (JANUARY 1988)]**PEER REVIEWED**

Laboratory Methods:

Clinical Laboratory Methods:

WHEN GAS CHROMATOGRAPHIC-MASS SPECTROSCOPY WAS USED IN ANALYSIS, **ETHYL ACETATE** WAS DETECTED IN ALL BLOOD SAMPLES & BRAIN TISSUES. THE CURVES OF BLOOD ETHYL ALCOHOL CONCN VS BLOOD PH VALUES SHOWED A REGRESSION DISTRIBUTION PATTERN. THESE RESULTS MAY BE USED IN FORENSIC INVESTIGATIONS.
[KOJIMA T ET AL; NIPPON HOIGAKU ZASSHI 34 (5): 587-95 (1980)]**PEER REVIEWED**

DETECTION & IDENTIFICATION OF VOLATILE ORGANIC COMPOUNDS, INCLUDING **ETHYL ACETATE,** IN WHOLE BLOOD, PLASMA, OR SERUM BY HEADSPACE GAS CHROMATOGRAPHY AS AN AID TO THE DIAGNOSIS OF SOLVENT ABUSE.
[RAMSEY JD, FLANAGAN RJ; J CHROMATOGR 240 (2): 423-44 (1982)]**PEER REVIEWED**

Analytic Laboratory Methods:

ANALYTE: **ETHYL ACETATE.** MATRIX: AIR. PROCEDURE: ADSORPTION ON CHARCOAL, DESORPTION WITH CARBON DISULFIDE, GAS CHROMATOGRAPHY. RANGE: 704-2950 MG/CU M.
[U.S. Department of Health, Education Welfare, Public Health Service. Center for Disease Control, National Institute for Occupational Safety Health. NIOSH Manual ofAnalytical Methods. 2nd ed. Volumes 1-7. Washington, DC: U.S. Government Printing Office, 1977-present.,p. V2 S49]**PEER REVIEWED**

Residual solvents in pharmaceutical powders were determined by gas chromatography with a headspace injection system. The chromatography conditions and parameters of the injection system were optimized to enable the quantification by external standardization of 21 most common solvents in concn ranging from a few ppm to a few percent. Porapak Q (100-120 mesh) was used as the stationary phase with flame ionization detection.
[Guimbard JP et al; J chromatogr 403: 109-21 (1987)]**PEER REVIEWED**

A generalized GC method is described for the determinations of a wide variety of residual solvents and other volatile impurities in bulk pharmaceuticals. ... Analytical data from replicated determinations of 7 representative cmpd are reported.
[Haky JE, Stickney TM; J Chromatogr 321 (1): 137-44 (1985)]**PEER

REVIEWED**

The head space method for determining volatile gases was developed and compared with results obtained by the conventional purge and trap method. A gas chromatogram fitted with a retractable retrofit on column injectors and split inlet systems was used. The more highly volatile compounds /including **ethyl acetate/** were clearly evident by the method but were lost to breakthrough in the purge and trap method. Head space samples generated contained appreciable amounts of water and were dominated by lower molecular weight compounds under normal conditions.
[Takeoka G, Jennings W; J Chromatrogr Sci 22 (5): 177-84 (1984)]**PEER REVIEWED**

Esters in distilled liquors, spectrophotometric method. Esters including **ethyl acetate** react quantitatively with hydroxylamine in alkaline solutions to form a hydroxamic acid which, forms colored complex with ferric ions. Ester concentration is proportional to absorbance at 525 nm at constant alcohol concentration and is calculated from standard curves.
[Association of Official Analytic Chemists. Official Methods of Analysis of the AOAC. 14th ed. Arlington, VA: Association of Official Analytic Chemists, Inc., 1984. 182]**PEER REVIEWED**

NIOSH Method 1457. Determination of **Ethyl Acetate** by Gas Chromatography with Flame Ionization Detection, GC/FID, workplace air, detection limit, 0.050 mg/cu m.
[U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSH Manual of Analytical Methods. 4th ed.Methods A-Z & Supplements. Washington, DC: U.S. Government Printing Office, Aug 1994.]**PEER REVIEWED**

AOAC Method 972.10. Alcohols (Higher) and **Ethyl Acetate** in Distilled Liquors. Alternative Gas Chromatographic Method.
[Association of Official Analytical Chemists. Official Methods of Analysis. 15th ed. and Supplements. Washington, DC: Association of Analytical Chemists, 1990 700]**PEER REVIEWED**

AOAC Method 968.09. Alcohols (Higher) and **Ethyl Acetate** in Distilled Liquors. Gas Chromatographic Method.
[Association of Official Analytical Chemists. Official Methods of Analysis. 15th ed. and Supplements. Washington, DC: Association of Analytical Chemists, 1990 700]**PEER REVIEWED**

Sampling Procedures:

ETHYL ACETATE VAPORS ARE ADSORBED ONTO SILICA GEL CONTAINED IN A LIGHTWEIGHT ALUMINUM ALLOY SAMPLING TUBE FOR USE IN DESORPTION AND ANALYTICAL TECHNIQUES.
[LEE GL, WALDRON T; ANN OCCUP HYG 19 (2): 129 (1976)]**PEER REVIEWED**

The field data of solvent concentrations were determined using active and passive samplers, and compared to values obtained from urinary analyses. Active samplers were taken by activated charcoal tubes; passive samples were taken by the TK200 passive dosimeters. /It was concluded/ that passive

dosimeters are reliable and represent a viable alternative for determination of solvents in air.
[Bartolucci GB; Ann Occup Hyg 30 (3): 295-306 (1986)]**PEER REVIEWED**

Analyte: **Ethyl acetate;** Matrix: Air; Procedure: Adsorption on charcoal. Sample size: 6 liters; Precision for total analytical and sampling method in the range of 704-2950 mg/cu m was 0.058, Flow rate: + or - 5 percent.
[U.S. Department of Health, Education Welfare, Public Health Service. Center for Disease Control, National Institute for Occupational Safety Health. NIOSH Manual ofAnalytical Methods. 2nd ed. Volumes 1-7. Washington, DC: U.S. Government Printing Office, 1977-present.,p. S49-1]**PEER REVIEWED**

Special References:

Synonyms and Identifiers:

Synonyms:

ACETATE D'ETHYLE (FRENCH)
PEER REVIEWED

Acetato de etilo (Spanish)
PEER REVIEWED

ACETIC ACID, ETHYL ESTER
PEER REVIEWED

ACETIC ETHER
PEER REVIEWED

Acetidin
PEER REVIEWED

Acetoxyethane
PEER REVIEWED

Aethylacetat (German)
PEER REVIEWED

AI3-00404
PEER REVIEWED

Caswell No 429
PEER REVIEWED

EPA Pesticide Chemical Code 044003
PEER REVIEWED

ESSIGESTER (GERMAN)
PEER REVIEWED

ETHYLACETAAT (DUTCH)
PEER REVIEWED

ETHYL ACETIC ESTER
PEER REVIEWED

ETHYLE (ACETATE D') (FRENCH)
PEER REVIEWED

ETHYL ESTER
PEER REVIEWED

ETHYLESTER KYSELINY OCTOVE (CZECH)
PEER REVIEWED

ETHYL ETHANOATE
PEER REVIEWED

ETILE (ACETATO DI) (ITALIAN)
PEER REVIEWED

OCTAN ETYLU (POLISH)
PEER REVIEWED

VINEGAR NAPHTHA
PEER REVIEWED

Formulations/Preparations:

GRADES: COMMERCIAL, 85-88%; 95-98%; 99%; NF /NATIONAL FORMULARY GRADE OF CHEMICAL/ (99%); FCC /FOOD CHEMICAL CODEX/.
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 12th ed. New York, NY: Van Nostrand Rheinhold Co., 1993 478]**PEER REVIEWED**

Nail polish remover typically 40 wt% **ethyl acetate.**
[Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984.,p. V7 163]**PEER REVIEWED**

Shipping Name/ Number DOT/UN/NA/IMO:

UN 1173; **Ethyl acetate**

IMO 3.2; **Ethyl acetate**

Standard Transportation Number:

49 091 60; **Ethyl acetate**

EPA Hazardous Waste Number:

U112; A toxic waste when a discarded commercial chemical product or manufacturing chemical intermediate or an off-specification commercial chemical product.

F003; A hazardous waste from nonspecific sources when a spent solvent.

RTECS Number:

NIOSH/AH5425000

Administrative Information:

Hazardous Substances Databank Number: 83

Last Revision Date: 20000313

Last Review Date: Reviewed by SRP on 5/7/1998

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Field Update on 01/18/1996, 1 field added/edited/deleted.
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Complete Update on 12/19/1994, 1 field added/edited/deleted.
Complete Update on 11/18/1994, 1 field added/edited/deleted.
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Complete Update on 08/04/1993, 1 field added/edited/deleted.
Field update on 12/10/1992, 1 field added/edited/deleted.
Complete Update on 11/20/1992, 1 field added/edited/deleted.
Complete Update on 04/27/1992, 1 field added/edited/deleted.
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Complete Update on 04/16/1990, 3 fields added/edited/deleted.
Complete Update on 01/11/1990, 2 fields added/edited/deleted.
Field update on 12/29/1989, 1 field added/edited/deleted.
Complete Update on 08/17/1989, 91 fields added/edited/deleted.
Complete Update on 10/03/1986

Record Length: 143454

ETHYL ACETATE

CASRN: 141-78-6

For other data, click on the Table of Contents

Human Health Effects:

Human Toxicity Excerpts:

STUDY OF 30 WORKERS EXPOSED CHRONICALLY TO 15-50 MG OF **ETHYL ACETATE** IN ADDITION TO 20 TO 80 MG OF AMYL ACETATE/L OF AIR SHOWED NO ... ABNORMALITIES IN CORNEA, MERELY HYPEREMIA OF BULBAR CONJUNCTIVA. ... PROLONGED INHALATION MAY BE DAMAGING TO LUNG, LIVER, KIDNEY, & HEART. ... NO EFFECT ON EYES ... KNOWN FROM SYSTEMIC ABSORPTION.

[Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986. 412]**PEER REVIEWED**

UNACCLIMATED SUBJECTS ... FOUND THE ODOR /OF **ETHYL ACETATE/** OBJECTIONABLY STRONG AT 200 PPM, AND MILD EYE, NOSE, AND THROAT IRRITATION AT 400 PPM.

[American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices. 5th ed. Cincinnati, OH:American Conference of Governmental Industrial Hygienists, 1986. 239]**PEER REVIEWED**

ETHYL ACETATE TESTED AT 10% IN PETROLATUM PRODUCED NO IRRITATION AFTER A 48-HOUR CLOSED PATCH TEST IN 25 HUMAN SUBJECTS. SENSITIZATION: A MAXIMIZATION TEST WAS CARRIED OUT ON 25 VOLUNTEERS. THE MATERIAL WAS TESTED AT A CONCN OF 10% IN PETROLATUM AND PRODUCED NO SENSITIZATION REACTIONS.

[Opdyke, D.L.J. (ed.). Monographs on Fragrance Raw Materials. New York: Pergamon Press, 1979. 341]**PEER REVIEWED**

SYMPTOMATOLOGY (acute intoxication): 1. Early emotional lability: exhilaration, boastfulness, talkativeness, remorse, and belligerency. 2. Impaired motor coordination: slowed reaction time, slurred speech, ataxia. 3. Sensory disturbances: diplopia, vertigo. 4. Flushing of face, rapid pulse, sweating. 5. Nausea and vomiting. Eventual incontinence of urine and feces. 6. Drowsiness, stupor, and finally coma, with impaired or absent tendon reflexes. Convulsive episodes may indicate hypoglycemia. 7. Pupils dilated or normal. 8. Peripheral vascular collapse (shock); hypotension, tachycardia, cold pale skin, hypothermia. 9. Slow stentorous respiration. 10. Death from respiratory or circulatory failure or from aspiration pneumonitis. 11. During convalescence: postalcoholic headache and gastritis; infections, alcoholic psychoses. /Ethyl alcohol/

[Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984.,p. III-169-70]**PEER REVIEWED**

Poison by inhalation. Moderately toxic by intraperitoneal and subcutaneous routes. Mildly toxic by ingestion. Human systemic effects by inhalation: olfactory changes, conjunctiva irritation, and

pulmonary changes. Human eye irritant. Irritating to mucous surfaces ... and is also mildly narcotic. On repeated or prolonged exposures, it causes conjunctival irritation and corneal clouding. High concentrations have a narcotic effect and can cause congestion of the liver and kidneys. Chronic poisoning has been described as producing anemia, leucocytosis (transient increase in the white blood cell count), and cloudy swelling, and fatty degeneration of the viscera.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1514]**PEER REVIEWED**

ETHYL ACETATE HAS ... REPUTATION OF BEING ONE OF THE LEAST TOXIC OF THE VOLATILE ORGANIC SOLVENTS.
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Volumes I,II, III. Cincinnati, OH: ACGIH, 1991. 569]**PEER REVIEWED**

IRRITANT EFFECT OF **ETHYL ACETATE** IS LESS STRONG THAN THAT OF PROPYL ACETATE OR BUTYL ACETATE.
[International Labour Office. Encyclopedia of Occupational Health and Safety. Volumes I and II. New York: McGraw-Hill Book Co., 1971. 477]**PEER REVIEWED**

... ALLEGED ILL EFFECTS OF **ETHYL ACETATE** HAVE OCCURRED DURING ITS INTENSIVE USE DURING EARLIER YEARS ... IMPURITIES MAY HAVE BEEN PRESENT OR IT MAY HAVE BEEN USED WITHOUT DUE CARE AND OFTEN IN COMBINATION WITH OTHER SOLVENTS.
[Snyder, R. (ed.). Ethel Browning's Toxicity and Metabolism of Industrial Solvents. Second Edition. Volume 3 Alcohols and Esters. New York, NY: Elsevier, 1992. 239]**PEER REVIEWED**

THE ALIPHATIC ESTERS USED AS LACQUER SOLVENTS, PRIMARILY **ETHYL ACETATE** AND BUTYL ACETATE, HAVE ... /SRP: CNS DEPRESSANT/ PROPERTIES WHICH ARE LESS PROMINENT THAN THOSE ASSOCIATED WITH THE CHLORINATED HYDROCARBONS.
[Hamilton, A., and H. L. Hardy. Industrial Toxicology. 3rd ed. Acton, Mass.: Publishing Sciences Group, Inc., 1974. 313]**PEER REVIEWED**

/Seventeen/ track team runners were evaluated after complaining of wheezing coughing, rhinitis, or shortness of breath after practicing in a facility under construction. Investigation revealed levels of **ethyl acetate** and toluene low enough to meet federal guidelines but apparently sufficient to cause symptoms in the athletes. Therefore, current standards for regulating potentially toxic organic chemicals may be inadequate when aerobic exercise is performed in the polluted environment.
[Larson DC; Physician Sportsmed 13 (1): 76-79 (1985)]**PEER REVIEWED**

A survey of the uptake of 5-hydroxytryptamine (serotonin) in platelets of workers exposed to organic solvents was conducted. Blood samples were obtained from six males, ages 34 to 58, employed in a graphic paint manufacturing facility and from 50 nonexposed individuals, 25 to 56 years old. Platelets were isolated and incubated with (14)carbon labeled serotonin. The uptake of radiolabeled serotonin, serum concentrations of calcium, potassium, and sodium ions, platelet count, and blood pH were also

determined. Breathing zone concentrations of organic solvents were obtained and analyzed by gas chromatography. The platelet count of the exposed workers was less than that of the comparisons. Maximal uptake rates of serotonin by platelets from the exposed workers was significantly greater than that of the comparisons. No significant differences in blood ion concentrations or pH values in the workers or comparisons were noted. The total concentration of organic solvents in the breathing zones of the exposed subjects ranged from 13 to 111 ppm. Compounds identified were 2 to 68 ppm toluene and 34 to 78 ppm **ethyl acetate. /**It was/ concluded that platelets of workers are affected by exposure to paint solvents.
[Beving H; Scand J Work Environ Health 10 (4): 229-34 (1984)]**PEER REVIEWED**

Ethyl acetate vapor is irritating to the eyes and respiratory passages of man at concentrations above 400 ppm. ... Due to its irritating properties, employees will not voluntarily remain in such high concentrations. ... This substance is a defatting agent, and prolonged exposure may cause irritation of the skin. Painful conjunctival irritation may occur from splashes in the eye. No chronic systemic effects have been reported in humans.
[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) PublicationNo. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981. 1]**PEER REVIEWED**

Overexposure to **ethyl acetate** may cause irritation of the eyes, nose, & throat. Severe overexposure may cause weakness, drowsiness, & unconsciousness.
[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) PublicationNo. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981.]**PEER REVIEWED**

Humans exposed to a concn of 400 ppm in 1.4 mg/l **ethyl acetate** for a short time were effected by nose and throat irritation. /From table/
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 2981]**PEER REVIEWED**

... **Ethyl acetate** is an irritant of the conjuctiva and mucous membrane of the respiratory tract. Animal experiments have shown that, at very high concentrations, the ester has /CNS depressant/ and lethal effects; at concentrations of 20000 to 43000 ppm, there may be pulmonary edema with hemorrhages, symptoms of central nervous system depression, secondary anemia and damage of the liver. In man, concentrations of 400 ppm cause irritation of the nose and pharynx; cases have also been known of irritation of the conjunctiva with temporary opacity of the cornea. In rare cases exposure may cause sensitization of the mucous membrane and eruptions of the skin. The irritant effect of **ethyl acetate** is less strong than that of propyl acetate or butyl acetate.
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 782]**PEER REVIEWED**

Skin, Eye and Respiratory Irritations:

Irritating to mucous surfaces, particularly the eyes, gums and respiratory passages ... . On repeated or prolonged exposures, it causes conjunctival irritation and corneal clouding.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1514]**PEER REVIEWED**

Medical Surveillance:

Consider the points of attack /eyes, skin, respiratory system/ in placement and periodic examinations.
[Sittig, M. Handbook of Toxic and Hazardous Chemicals and Carcinogens, 1985. 2nd ed. Park Ridge, NJ: Noyes Data Corporation, 1985. 408]**PEER REVIEWED**

Whole Blood: Reference Ranges: Normal - Not established; Exposed - Not established; Toxic - Not stablished.
[Ryan, R.P., C.E. Terry (eds.). Toxicology Desk Reference 4th ed. Volumes 1-3. Taylor & Francis, washington, D.C. 1997. 1256]**PEER REVIEWED**

Serum or Plasma: Reference Ranges: Normal - Not established; Exposed - Not established; Toxic - Not stablished.
[Ryan, R.P., C.E. Terry (eds.). Toxicology Desk Reference 4th ed. Volumes 1-3. Taylor & Francis, washington, D.C. 1997. 1256]**PEER REVIEWED**

Urine: Reference Ranges: Normal - Not established; Exposed - Not established; Toxic - Not stablished.
[Ryan, R.P., C.E. Terry (eds.). Toxicology Desk Reference 4th ed. Volumes 1-3. Taylor & Francis, washington, D.C. 1997. 1256]**PEER REVIEWED**

Respiratory Symptom Questionnaires: Questionnaires have been published by the American Thoracic Society and the British Medical Research Council. These questionnaires have been found to be useful in identification of people with chronic bronchitis, however certain pulmonary function tests such as FEV 1 have been found to be better predictors of chronic airflow obstruction.
[Ryan, R.P., C.E. Terry (eds.). Toxicology Desk Reference 4th ed. Volumes 1-3. Taylor & Francis, washington, D.C. 1997. 1257]**PEER REVIEWED**

Chest Radiography: This test is widely used for assessing pulmonary disease. Chest radiographs have been found to be useful for detection of early lung cancer in asymptomatic people, especially for detection of peripheral tumors such as adenocarcinomas. However, even though OSHA mandates this test for exposure to some toxicants such as asbestos, there are conflicting views on its efficacy in detection of pulmonary disease.
[Ryan, R.P., C.E. Terry (eds.). Toxicology Desk Reference 4th ed. Volumes 1-3. Taylor & Francis, washington, D.C. 1997. 1257]**PEER REVIEWED**

Pulmonary Function Tests: The tests that have been found to be practical for population monitoring include: Spirometry and expiratory flow-volume curves; Determination of lung volumes; Diffusing

capacity for carbon monoxide; Single-breath nitrogen washout; Inhalation challenge tests; Serial measurements of peak expiratory flow; Exercise testing.
[Ryan, R.P., C.E. Terry (eds.). Toxicology Desk Reference 4th ed. Volumes 1-3. Taylor & Francis, washington, D.C. 1997. 1257]**PEER REVIEWED**

Sputum Cytology: Sputum cytology along with chest radiographs have been the standard procedures for detecting early lung cancer in asymptomatic patients. Sputum cytology has been found to be useful for detection of central tumors, especially squamous carcinomas. For this test to be effective, exfoliated respiratory mucosal cells must be present in the expectorated specimen. Pooling of sputum collected over 2-3 days may enhance the sensitivity of this test by increasing the yield of exfoliated cells in the specimen.
[Ryan, R.P., C.E. Terry (eds.). Toxicology Desk Reference 4th ed. Volumes 1-3. Taylor & Francis, washington, D.C. 1997. 1257]**PEER REVIEWED**

Evaluation of Peripheral Neuropathy: Nerve conduction study; Electromyography; Quantitative sensory testing; Thermography.
[Ryan, R.P., C.E. Terry (eds.). Toxicology Desk Reference 4th ed. Volumes 1-3. Taylor & Francis, washington, D.C. 1997. 1258]**PEER REVIEWED**

Evaluation of Central Nervous System Effects: Evaluation of CNS effects can be performed through neuropsychological assessment, which consists of a clinical interview and administration of standardized personality and neuropsychological tests. The areas that the neuropsychology test batteries focus on include the domains of memory and attention; visuoperceptual, visual scanning, visuospatial, and visual memory; and motor speed and reaction time. There is limited data on which components of the test batteries are best indicators of early CNS effects.
[Ryan, R.P., C.E. Terry (eds.). Toxicology Desk Reference 4th ed. Volumes 1-3. Taylor & Francis, washington, D.C. 1997. 1258]**PEER REVIEWED**

Evaluation of Cranial Neuropathies: Evaluation of cranial nerve damage, as evidenced by symptoms such as loss of balance, visual function, smell, taste, or sensation on the face, can be accomplished through a physical examination focusing on tests such as: Smell assessment - standardized odor threshold and identification testing; Vision assessment - standard acuity tests, visual field tests, contrast sensitivity, and color vision measurements (vision assessment); Facial and Trigeminal Nerve assessment - blink reflex (pontogram); Vestibular assessment - pure tone audiometry for bone- and air-conducted sounds, threshold decay at 4 kHz, speech discrimination and speech reception thresholds, tympanograms and acoustic thresholds, electronystagmograms; Hearing assessment - audiometry testing.
[Ryan, R.P., C.E. Terry (eds.). Toxicology Desk Reference 4th ed. Volumes 1-3. Taylor & Francis, washington, D.C. 1997. 1258]**PEER REVIEWED**

Populations at Special Risk:

Employees /with chronic respiratory, skin, liver, or kidney disase may be/ at increased risk from **ethyl acetate.**

[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) PublicationNo. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981. 1]**PEER REVIEWED**

Probable Routes of Human Exposure:

NIOSH (NOES Survey 1981-1983) has statistically estimated that 375,906 workers (87,691 of these are female) are potentially exposed to **ethyl acetate** in the US(1). Occupational exposure to **ethyl acetate** may occur through inhalation and dermal contact with this compound at workplaces where **ethyl acetate** is produced or used(SRC). **Ethyl acetate** was identified (relative abundance) in air samples collected where printing pastes (66%) and paints (30%) were used, in car repair shops (45%), and in various other industries (57%) in Belgium(2). Mean concentrations of **ethyl acetate** in air during parquet work in Finland were 119 ppm during installation with resin adhesives; 319 ppm during puttying; 72 ppm during sanding after puttying; 413 ppm during undercoat varnishing (nitrocellulose); 64 ppm during urea-formaldehyde varnishing; and 1 ppm during work with water-based varnishes(3). It was also detected in air during the use of contact adhesives at mean concentrations of 14 ppm during repair of a textile carpet (dispersion and contact adhesives); 83 ppm during repair of a textile carpet (contact adhesives only); 29 ppm during beading of textile carpets (contact adhesives only); and 71 ppm during repair of bathroom floor mats (dispersion and contact adhesives)(3). **Ethyl acetate** was detected in 36% of all air samples, at a mean concentration of 11 ppm, collected from Finnish furniture factories from 1975 to 1984(4). Breathing zone samples collected during spray painting contained **ethyl acetate** at a geometric mean concentration of 9.51 ppm(5). It was detected in the air of one auto paint shop at a concentration of 10.5 mg/cu m(6). **Ethyl acetate** was identified in 12% of 275 products (including thinners, degreasers, paints, inks, and dome reagents) used in workplaces in various industries(7). **Ethyl acetate** was identified in the breathing zone of shoe factory workers(8). **Ethyl acetate** was detected in the ambient air of shoe factory in Italy in Nov 1991 at median concentrations of 10 and 7 mg/cu m(9).
[(1) NIOSH; National Occupational Exposure Survey (NOES) (1983) (2) Veulemans H et al; Am Indust Hyg Assoc J 48: 671-7 (1987) (3) Riala REE, Riihimaki HA; Appl Occup Environ Hyg 6: 301-8 (1991) (4) Priha E; Ann Occup Hyg 30: 289-94 (1986) (5) Myer HE et al; Am Ind Hyg Assoc J 54: 663-70 (1993) (6) Medinilla J, Espigares M; Ann Occup Hyg 32: 509-13 (1988) (7) Lehman E et al; pp. 31-41 in Safety and Health ASP Org Sol Expos Finland April 1985, Riihimaki V, Ulfvarson U, eds NY,NY: Alan R Liss Inc (1986) (8) Ahonen I, Schimberg RW; Br J Ind Med 45: 133-6 (1988) (9) Mutti A et al; Int Arch Occup Environ Health 65: S171-6 (1993)]**PEER REVIEWED**

The general population may be exposed to **ethyl acetate** via inhalation of ambient air, ingestion of food and drinking water, and dermal contact with consumer products containing **ethyl acetate. (**SRC)
PEER REVIEWED

Body Burden:

Mother's milk from 4 urban areas in the USA, 1 of 8 samples positive(1). 7 out of 12 breath samples collected from nine volunteers in Bayonne and Elizabeth, NJ between July and Dec 1980 contained **ethyl acetate** at unreported concentrations(2). **Ethyl acetate** was identified as a component in 13.7% of

expired air samples from 54 volunteers in the Chicago area at a geometric mean concentration of 0.447 ng/l(3). **Ethyl acetate** was detected in expired air samples from 5 of 8 male volunteers at levels ranging from 0.30 to 190.0 ug/hr(4).
[(1) Pellizzari ED et al; Environ Sci Technol 16: 781-5 (1982) (2) Wallace LA et al; Environ Res 35: 293-319 (1984) (3) Krotoszynski BK et al; J Anal Toxicol 3: 225-34 (1979) (4) Conkle JP et al; Arch Environ Health 30: 290-5 (1975)]**PEER REVIEWED**

ETHYL ACETATE

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[Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984.,p. III-169-70]**PEER REVIEWED**

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[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1514]**PEER REVIEWED**

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... ALLEGED ILL EFFECTS OF **ETHYL ACETATE** HAVE OCCURRED DURING ITS INTENSIVE USE DURING EARLIER YEARS ... IMPURITIES MAY HAVE BEEN PRESENT OR IT MAY HAVE BEEN USED WITHOUT DUE CARE AND OFTEN IN COMBINATION WITH OTHER SOLVENTS.
[Snyder, R. (ed.). Ethel Browning's Toxicity and Metabolism of Industrial Solvents. Second Edition. Volume 3 Alcohols and Esters. New York, NY: Elsevier, 1992. 239]**PEER REVIEWED**

THE ALIPHATIC ESTERS USED AS LACQUER SOLVENTS, PRIMARILY **ETHYL ACETATE** AND BUTYL ACETATE, HAVE ... /SRP: CNS DEPRESSANT/ PROPERTIES WHICH ARE LESS PROMINENT THAN THOSE ASSOCIATED WITH THE CHLORINATED HYDROCARBONS.
[Hamilton, A., and H. L. Hardy. Industrial Toxicology. 3rd ed. Acton, Mass.: Publishing Sciences Group, Inc., 1974. 313]**PEER REVIEWED**

/Seventeen/ track team runners were evaluated after complaining of wheezing coughing, rhinitis, or shortness of breath after practicing in a facility under construction. Investigation revealed levels of **ethyl acetate** and toluene low enough to meet federal guidelines but apparently sufficient to cause symptoms in the athletes. Therefore, current standards for regulating potentially toxic organic chemicals may be inadequate when aerobic exercise is performed in the polluted environment.
[Larson DC; Physician Sportsmed 13 (1): 76-79 (1985)]**PEER REVIEWED**

A survey of the uptake of 5-hydroxytryptamine (serotonin) in platelets of workers exposed to organic solvents was conducted. Blood samples were obtained from six males, ages 34 to 58, employed in a graphic paint manufacturing facility and from 50 nonexposed individuals, 25 to 56 years old. Platelets were isolated and incubated with (14)carbon labeled serotonin. The uptake of radiolabeled serotonin, serum concentrations of calcium, potassium, and sodium ions, platelet count, and blood pH were also determined. Breathing zone concentrations of organic solvents were obtained and analyzed by gas chromatography. The platelet count of the exposed workers was less than that of the comparisons. Maximal uptake rates of serotonin by platelets from the exposed workers was significantly greater than

that of the comparisons. No significant differences in blood ion concentrations or pH values in the workers or comparisons were noted. The total concentration of organic solvents in the breathing zones of the exposed subjects ranged from 13 to 111 ppm. Compounds identified were 2 to 68 ppm toluene and 34 to 78 ppm **ethyl acetate. /**It was/ concluded that platelets of workers are affected by exposure to paint solvents.
[Beving H; Scand J Work Environ Health 10 (4): 229-34 (1984)]**PEER REVIEWED**

Ethyl acetate vapor is irritating to the eyes and respiratory passages of man at concentrations above 400 ppm. ... Due to its irritating properties, employees will not voluntarily remain in such high concentrations. ... This substance is a defatting agent, and prolonged exposure may cause irritation of the skin. Painful conjunctival irritation may occur from splashes in the eye. No chronic systemic effects have been reported in humans.
[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) PublicationNo. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981. 1]**PEER REVIEWED**

Overexposure to **ethyl acetate** may cause irritation of the eyes, nose, & throat. Severe overexposure may cause weakness, drowsiness, & unconsciousness.
[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) PublicationNo. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981.]**PEER REVIEWED**

Humans exposed to a concn of 400 ppm in 1.4 mg/l **ethyl acetate** for a short time were effected by nose and throat irritation. /From table/
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 2981]**PEER REVIEWED**

... **Ethyl acetate** is an irritant of the conjuctiva and mucous membrane of the respiratory tract. Animal experiments have shown that, at very high concentrations, the ester has /CNS depressant/ and lethal effects; at concentrations of 20000 to 43000 ppm, there may be pulmonary edema with hemorrhages, symptoms of central nervous system depression, secondary anemia and damage of the liver. In man, concentrations of 400 ppm cause irritation of the nose and pharynx; cases have also been known of irritation of the conjunctiva with temporary opacity of the cornea. In rare cases exposure may cause sensitization of the mucous membrane and eruptions of the skin. The irritant effect of **ethyl acetate** is less strong than that of propyl acetate or butyl acetate.
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 782]**PEER REVIEWED**

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Skin, Eye and Respiratory Irritations:

Irritating to mucous surfaces, particularly the eyes, gums and respiratory passages ... . On repeated or prolonged exposures, it causes conjunctival irritation and corneal clouding.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1514]**PEER REVIEWED**

ETHYL ACETATE

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For other data, click on the Table of Contents

Medical Surveillance:

Consider the points of attack /eyes, skin, respiratory system/ in placement and periodic examinations.
[Sittig, M. Handbook of Toxic and Hazardous Chemicals and Carcinogens, 1985. 2nd ed. Park Ridge, NJ: Noyes Data Corporation, 1985. 408]**PEER REVIEWED**

Whole Blood: Reference Ranges: Normal - Not established; Exposed - Not established; Toxic - Not stablished.
[Ryan, R.P., C.E. Terry (eds.). Toxicology Desk Reference 4th ed. Volumes 1-3. Taylor & Francis, washington, D.C. 1997. 1256]**PEER REVIEWED**

Serum or Plasma: Reference Ranges: Normal - Not established; Exposed - Not established; Toxic - Not stablished.
[Ryan, R.P., C.E. Terry (eds.). Toxicology Desk Reference 4th ed. Volumes 1-3. Taylor & Francis, washington, D.C. 1997. 1256]**PEER REVIEWED**

Urine: Reference Ranges: Normal - Not established; Exposed - Not established; Toxic - Not stablished.
[Ryan, R.P., C.E. Terry (eds.). Toxicology Desk Reference 4th ed. Volumes 1-3. Taylor & Francis, washington, D.C. 1997. 1256]**PEER REVIEWED**

Respiratory Symptom Questionnaires: Questionnaires have been published by the American Thoracic Society and the British Medical Research Council. These questionnaires have been found to be useful in identification of people with chronic bronchitis, however certain pulmonary function tests such as FEV 1 have been found to be better predictors of chronic airflow obstruction.
[Ryan, R.P., C.E. Terry (eds.). Toxicology Desk Reference 4th ed. Volumes 1-3. Taylor & Francis, washington, D.C. 1997. 1257]**PEER REVIEWED**

Chest Radiography: This test is widely used for assessing pulmonary disease. Chest radiographs have been found to be useful for detection of early lung cancer in asymptomatic people, especially for detection of peripheral tumors such as adenocarcinomas. However, even though OSHA mandates this test for exposure to some toxicants such as asbestos, there are conflicting views on its efficacy in detection of pulmonary disease.
[Ryan, R.P., C.E. Terry (eds.). Toxicology Desk Reference 4th ed. Volumes 1-3. Taylor & Francis, washington, D.C. 1997. 1257]**PEER REVIEWED**

Pulmonary Function Tests: The tests that have been found to be practical for population monitoring include: Spirometry and expiratory flow-volume curves; Determination of lung volumes; Diffusing capacity for carbon monoxide; Single-breath nitrogen washout; Inhalation challenge tests; Serial

measurements of peak expiratory flow; Exercise testing.
[Ryan, R.P., C.E. Terry (eds.). Toxicology Desk Reference 4th ed. Volumes 1-3. Taylor & Francis, washington, D.C. 1997. 1257]**PEER REVIEWED**

Sputum Cytology: Sputum cytology along with chest radiographs have been the standard procedures for detecting early lung cancer in asymptomatic patients. Sputum cytology has been found to be useful for detection of central tumors, especially squamous carcinomas. For this test to be effective, exfoliated respiratory mucosal cells must be present in the expectorated specimen. Pooling of sputum collected over 2-3 days may enhance the sensitivity of this test by increasing the yield of exfoliated cells in the specimen.
[Ryan, R.P., C.E. Terry (eds.). Toxicology Desk Reference 4th ed. Volumes 1-3. Taylor & Francis, washington, D.C. 1997. 1257]**PEER REVIEWED**

Evaluation of Peripheral Neuropathy: Nerve conduction study; Electromyography; Quantitative sensory testing; Thermography.
[Ryan, R.P., C.E. Terry (eds.). Toxicology Desk Reference 4th ed. Volumes 1-3. Taylor & Francis, washington, D.C. 1997. 1258]**PEER REVIEWED**

Evaluation of Central Nervous System Effects: Evaluation of CNS effects can be performed through neuropsychological assessment, which consists of a clinical interview and administration of standardized personality and neuropsychological tests. The areas that the neuropsychology test batteries focus on include the domains of memory and attention; visuoperceptual, visual scanning, visuospatial, and visual memory; and motor speed and reaction time. There is limited data on which components of the test batteries are best indicators of early CNS effects.
[Ryan, R.P., C.E. Terry (eds.). Toxicology Desk Reference 4th ed. Volumes 1-3. Taylor & Francis, washington, D.C. 1997. 1258]**PEER REVIEWED**

Evaluation of Cranial Neuropathies: Evaluation of cranial nerve damage, as evidenced by symptoms such as loss of balance, visual function, smell, taste, or sensation on the face, can be accomplished through a physical examination focusing on tests such as: Smell assessment - standardized odor threshold and identification testing; Vision assessment - standard acuity tests, visual field tests, contrast sensitivity, and color vision measurements (vision assessment); Facial and Trigeminal Nerve assessment - blink reflex (pontogram); Vestibular assessment - pure tone audiometry for bone- and air-conducted sounds, threshold decay at 4 kHz, speech discrimination and speech reception thresholds, tympanograms and acoustic thresholds, electronystagmograms; Hearing assessment - audiometry testing.
[Ryan, R.P., C.E. Terry (eds.). Toxicology Desk Reference 4th ed. Volumes 1-3. Taylor & Francis, washington, D.C. 1997. 1258]**PEER REVIEWED**

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Populations at Special Risk:

Employees /with chronic respiratory, skin, liver, or kidney disase may be/ at increased risk from **ethyl acetate.**

[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) PublicationNo. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981. 1]**PEER REVIEWED**

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Probable Routes of Human Exposure:

NIOSH (NOES Survey 1981-1983) has statistically estimated that 375,906 workers (87,691 of these are female) are potentially exposed to **ethyl acetate** in the US(1). Occupational exposure to **ethyl acetate** may occur through inhalation and dermal contact with this compound at workplaces where **ethyl acetate** is produced or used(SRC). **Ethyl acetate** was identified (relative abundance) in air samples collected where printing pastes (66%) and paints (30%) were used, in car repair shops (45%), and in various other industries (57%) in Belgium(2). Mean concentrations of **ethyl acetate** in air during parquet work in Finland were 119 ppm during installation with resin adhesives; 319 ppm during puttying; 72 ppm during sanding after puttying; 413 ppm during undercoat varnishing (nitrocellulose); 64 ppm during urea-formaldehyde varnishing; and 1 ppm during work with water-based varnishes(3). It was also detected in air during the use of contact adhesives at mean concentrations of 14 ppm during repair of a textile carpet (dispersion and contact adhesives); 83 ppm during repair of a textile carpet (contact adhesives only); 29 ppm during beading of textile carpets (contact adhesives only); and 71 ppm during repair of bathroom floor mats (dispersion and contact adhesives)(3). **Ethyl acetate** was detected in 36% of all air samples, at a mean concentration of 11 ppm, collected from Finnish furniture factories from 1975 to 1984(4). Breathing zone samples collected during spray painting contained **ethyl acetate** at a geometric mean concentration of 9.51 ppm(5). It was detected in the air of one auto paint shop at a concentration of 10.5 mg/cu m(6). **Ethyl acetate** was identified in 12% of 275 products (including thinners, degreasers, paints, inks, and dome reagents) used in workplaces in various industries(7). **Ethyl acetate** was identified in the breathing zone of shoe factory workers(8). **Ethyl acetate** was detected in the ambient air of shoe factory in Italy in Nov 1991 at median concentrations of 10 and 7 mg/cu m(9).
[(1) NIOSH; National Occupational Exposure Survey (NOES) (1983) (2) Veulemans H et al; Am Indust Hyg Assoc J 48: 671-7 (1987) (3) Riala REE, Riihimaki HA; Appl Occup Environ Hyg 6: 301-8 (1991) (4) Priha E; Ann Occup Hyg 30: 289-94 (1986) (5) Myer HE et al; Am Ind Hyg Assoc J 54: 663-70 (1993) (6) Medinilla J, Espigares M; Ann Occup Hyg 32: 509-13 (1988) (7) Lehman E et al; pp. 31-41 in Safety and Health ASP Org Sol Expos Finland April 1985, Riihimaki V, Ulfvarson U, eds NY,NY: Alan R Liss Inc (1986) (8) Ahonen I, Schimberg RW; Br J Ind Med 45: 133-6 (1988) (9) Mutti A et al; Int Arch Occup Environ Health 65: S171-6 (1993)]**PEER REVIEWED**

The general population may be exposed to **ethyl acetate** via inhalation of ambient air, ingestion of food and drinking water, and dermal contact with consumer products containing **ethyl acetate. (**SRC)
PEER REVIEWED

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Body Burden:

Mother's milk from 4 urban areas in the USA, 1 of 8 samples positive(1). 7 out of 12 breath samples collected from nine volunteers in Bayonne and Elizabeth, NJ between July and Dec 1980 contained **ethyl acetate** at unreported concentrations(2). **Ethyl acetate** was identified as a component in 13.7% of expired air samples from 54 volunteers in the Chicago area at a geometric mean concentration of 0.447 ng/l(3). **Ethyl acetate** was detected in expired air samples from 5 of 8 male volunteers at levels ranging from 0.30 to 190.0 ug/hr(4).

[(1) Pellizzari ED et al; Environ Sci Technol 16: 781-5 (1982) (2) Wallace LA et al; Environ Res 35: 293-319 (1984) (3) Krotoszynski BK et al; J Anal Toxicol 3: 225-34 (1979) (4) Conkle JP et al; Arch Environ Health 30: 290-5 (1975)]**PEER REVIEWED**

ETHYL ACETATE

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Emergency Medical Treatment:

Emergency Medical Treatment:

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The following Overview, *** **ETHYL ACETATE ***,** is relevant for this HSDB record chemical.

Life Support:

```
  o   This overview assumes that basic life support measures
      have been instituted.
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Clinical Effects:

```
SUMMARY OF EXPOSURE
 0.2.1.1 ACUTE EXPOSURE
   o   Ethyl acetate is low in toxicity.  It is a mild mucous
       membrane irritant, but is not caustic.  In high
       concentrations it may be a CNS depressant.  Animal
       studies have demonstrated pulmonary edema, decreased
       cardiac contractility, seizures and hepatic damage, but
       these have NOT been reported in humans.
 0.2.1.2 CHRONIC EXPOSURE
   o   Chronic poisoning has been described as producing
       anemia, leucocytosis (transient increase in the white
       blood cell count) and cloudy swelling, and fatty
       degeneration of the viscera in animal studies (Sax &
       Lewis, 1989).
HEENT
 0.2.4.1 ACUTE EXPOSURE
   o   Ethyl acetate is irritating to the conjunctivae but
       leaves no residual effects.  Nose and throat irritation
       is seen at levels greater than 400 ppm for 3 to 5
       minutes.
NEUROLOGIC
 0.2.7.1 ACUTE EXPOSURE
   o   Chronic exposure to solvent mixtures including ethyl
```

acetate has been associated with poorer performance on neurobehavioral tests. High concentrations orally administered to rabbits caused lack of coordination. High concentrations have intoxicating properties in animals and would be expected to cause narcosis in humans.

DERMATOLOGIC

0.2.14.1 ACUTE EXPOSURE

- Drying as well as skin defatting and cracking may be seen with dermal application. Sensitizations to **ethyl acetate** have been reported but are rare.

Laboratory:

- Various techniques are available, primarily using gas chromatography or spectrometric techniques. Toxic levels have not been established.

Treatment Overview:

SUMMARY EXPOSURE

- Because of rapid hydrolysis and low toxicity, inhalation or ingestion of ethyl acetates seldom requires treatment. Patients should be monitored for CNS depression if large amounts have been ingested.

ORAL EXPOSURE

- Emesis or activated charcoal is unlikely to be necessary due to the low toxicity of these compounds.
- No specific antidotes or treatments are available. Monitor patients ingesting large amounts for CNS depression, respiratory depression, and decreased cardiac contractility.

INHALATION EXPOSURE

- DECONTAMINATION: Move patient to fresh air. Monitor for respiratory distress. If cough or difficulty in breathing develops, evaluate for respiratory tract irritation, bronchitis, or pneumonitis. Administer 100 percent humidified supplemental oxygen with assisted ventilation as required.

EYE EXPOSURE

- DECONTAMINATION: Exposed eyes should be irrigated with copious amounts of tepid water for at least 15 minutes. If irritation, pain, swelling, lacrimation, or photophobia persist, the patient should be seen in a health care facility.

DERMAL EXPOSURE

- DECONTAMINATION: Wash exposed area extremely thoroughly

with soap and water. A physician may need to examine the area if irritation or pain persists.

Range of Toxicity:

- No adverse symptoms were noted in workers exposed to 375 to 1,500 ppm for several months. Humans find concentrations greater than 200 ppm objectionable because of the strong odor. 400 ppm caused nose and throat irritation. The TLV is 400 ppm (1,400 mg/m(3)).

[Rumack BH: POISINDEX(R) Information System. Micromedex, Inc., Englewood, CO, 2001; CCIS Volume 107, edition exp February, 2001. Hall AH & Rumack BH (Eds):TOMES(R) Information System. Micromedex, Inc., Englewood, CO, 2001; CCIS Volume 107, edition exp February, 2001.] **PEER REVIEWED**

Antidote and Emergency Treatment:

For basic treatment: Establish a patent airway. Suction if necessary. Watch for signs of respiratory insufficiency and assist ventilations if necessary. Administer oxygen by nonrebreather mask at 10 to 15 L/min. Monitor for pulmonary edema and treat if necessary ... . Monitor for shock and treat if necessary ... . For eye contamination, flush eyes immediately with water. Irrigate each eye continuously with normal saline during transport ... . Do not use emetics. For ingestion, administer activated charcoal ... . /Esters and related compounds/

[Bronstein, A.C., P.L. Currance; Emergency Care for Hazardous Materials Exposure. 2nd ed. St. Louis, MO. Mosby Lifeline. 1994. 221]**PEER REVIEWED**

For advanced treatment: Consider orotracheal or nasotracheal intubation for airway control in the patient who is unconscious. Positive-pressure ventilation techniques with a bag-valve-mask device may be beneficial. Monitor cardiac rhythm and treat arrhythmias if necessary ... . Start an IV with D5W TKO /SRP: To keep open, "minimal flow rate"/. Ringer's if signs of hypovolemia are present. Watch for signs of fluid overload. For hypotension with signs of hypovolemia, administer fluid cautiously. Consider vasopressors if patient is hypotensive with a normal fluid volume. Watch for signs of fluid overload ... . Consider drug therapy for pulmonary edema ... . Use proparacaine hydrochloride to assist eye irrigation ... . /Esters and related compounds/

[Bronstein, A.C., P.L. Currance; Emergency Care for Hazardous Materials Exposure. 2nd ed. St. Louis, MO. Mosby Lifeline. 1994.,p. 221-2]**PEER REVIEWED**

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Emergency Medical Treatment:

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0.2.1.2 CHRONIC EXPOSURE

- Chronic poisoning has been described as producing anemia, leucocytosis (transient increase in the white blood cell count) and cloudy swelling, and fatty degeneration of the viscera in animal studies (Sax & Lewis, 1989).

HEENT

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NEUROLOGIC

0.2.7.1 ACUTE EXPOSURE

- Chronic exposure to solvent mixtures including **ethyl acetate** has been associated with poorer performance on neurobehavioral tests. High concentrations orally

administered to rabbits caused lack of coordination. High concentrations have intoxicating properties in animals and would be expected to cause narcosis in humans.

DERMATOLOGIC

0.2.14.1 ACUTE EXPOSURE

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[Bronstein, A.C., P.L. Currance; Emergency Care for Hazardous Materials Exposure. 2nd ed. St. Louis, MO. Mosby Lifeline. 1994.,p. 221-2]**PEER REVIEWED**

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Animal Toxicity Studies:

Non-Human Toxicity Excerpts:

ANIMAL EXPERIMENTS HAVE SHOWN THAT, IN VERY HIGH CONCN, THE ESTER HAS ... /SRP: CNS DEPRESSANT/ & LETHAL EFFECTS.
[International Labour Office. Encyclopedia of Occupational Health and Safety. Volumes I and II. New York: McGraw-Hill Book Co., 1971. 477]**PEER REVIEWED**

... ANIMALS COULD WITHSTAND CONCN OF **ETHYL ACETATE** OF 2000 PPM FOR 65, 4 HR EXPOSURES WITHOUT APPARENT ILL EFFECTS AS MEASURED BY LACK OF CHANGE IN BODY WT & IN RED & WHITE BLOOD COUNTS.
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Volumes I,II, III. Cincinnati, OH: ACGIH, 1991. 569]**PEER REVIEWED**

CHRONIC, REPEATED INHALATION BY MICE 6 HR/DAY FOR 7 DAYS OF 4200-4400 PPM /& BY GUINEA PIGS OF 2000 PPM/ WAS FOUND ... TO CAUSE NO DEFINITE ... /SRP: CNS DEPRESSANT/ SYMPTOMS, BUT ... NOTED INCR IN ERYTHROCYTES WITH NO CORRESPONDING INCR IN HEMOGLOBIN, & SOME INCR IN POLYMORPHS. ... THERE WAS LOSS OF APPETITE ... NO CHANGE IN ... URINE ... .
[Snyder, R. (ed.). Ethel Browning's Toxicity and Metabolism of Industrial Solvents. Second Edition. Volume 3 Alcohols and Esters. New York, NY: Elsevier, 1992. 239]**PEER REVIEWED**

... SALIVATION, COUGHING, ... PAIN, & FOLLOWED BY DEATH OF 25% OF ANIMALS DURING PERIOD OF DEEP /SRP: CNS DEPRESSION/ ...
[Snyder, R. (ed.). Ethel Browning's Toxicity and Metabolism of Industrial Solvents. Second Edition. Volume 3 Alcohols and Esters. New York, NY: Elsevier, 1992. 239]**PEER REVIEWED**

... EXPOSURE OF RABBITS TO VAPOR AT CONCN WHICH WOULD BE SCARCELY TOLERABLE TO HUMAN BEINGS CAUSED NO CORNEAL DAMAGE DESPITE EXPOSURE FOR 8 HR A DAY, 5 DAYS A WK, FOR ... UP TO 7 WK. ONLY CONJUNCTIVAE GAVE INDICATIONS OF IRRITATION ... STD TESTING ON RABBIT EYES ... RESULTED IN RATING OF 2 ON SCALE OF 10 /10 MOST SEVERE/ ... .
[Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986. 239]**PEER REVIEWED**

WHEN **ETHYL ACETATE** WAS INJECTED INTO THE YOLK SAC OF FRESH FERTILE CHICKEN EGGS BEFORE INCUBATION IN A DOSE OF 9, 22.5, 45, OR 90 MG/EGG, THE HATCHABILITIES WERE 85, 50, 35, AND 15%, RESPECTIVELY.

[Opdyke, D.L.J. (ed.). Monographs on Fragrance Raw Materials. New York: Pergamon Press, 1979. 341]**PEER REVIEWED**

EXPOSURE OF THE FISH /COMMON INDIAN CATFISH, HETEROPNEUSTES FOSSILUS/ TO 170 PPM OF **ETHYL ACETATE** FOR 3, 6, 12, 48, & 96 HR INDUCED MARKED CHANGES IN CARBOHYDRATE METABOLISM. HEPATIC GLYCOGEN LEVELS DECLINED SIGNIFICANTLY AT 3, 48, & 96 HR, BUT THERE WAS NO MARKED ALTERATION IN MUSCLE GLYCOGEN CONTENT AT ANY OF THE EXPOSURE PERIODS. HYPERGLYCEMIA OCCURRED AT ALL TIME INTERVALS. BLOOD PYRUVATE LEVELS WERE ELEVATED AT 3, 6, 48, & 96 HR. HYPERLACTICEMIA RESULTED AT 3 & 96 HR, BUT HYPOLACTICEMIA OCCURRED AT 6 & 12 HR. IMPAIRMENT OF CARBOHYDRATE METABOLISM MIGHT BE RESPONSIBLE FOR THE TOXIC ACTION OF **ETHYL ACETATE.**
[GUPTA AB, SRIVASTAVA AK; ECOTOXICOL ENVIRON SAF 6 (2): 166-70 (1982)]**PEER REVIEWED**

Ethyl acetate was negative for mutagenicity in Salmonella typhimurium assays.
[NTP; Fiscal Year 1987 Annual Plan p.70 (1987) NTP-87-001]**PEER REVIEWED**

Toxicity Rating: 3. Relatively innocuous, lying on the borderline between toxicity classes 2 and 3. Mild local irritation and central nervous depression. On a molar basis the simple esters of ethyl alcohol are more toxic than ethanol by 4 to 10-fold. ... Toxicity appears to be due to unhydrolyzed esters and not to ethyl alcohol.
[Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984.,p. II-201]**PEER REVIEWED**

... In animals it has a narcotic effect at concentrations of over 5000 ppm. ... Repeated exposures of rabbits to 4450 ppm for 1 hr daily for 40 days resulted in anemia with leukocytosis, and damage to liver and kidneys. Animals exposed to lethal concentrations died with pulmonary edema and hemorrhage. ...
[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) PublicationNo. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981. 1]**PEER REVIEWED**

Cats exposed to a concn of 12,000 ppm in 43 mg/l for 5 hr were affected by the lowest /SRP: CNS depressant/ concn. Exposures to 20,000 ppm in 72 mg/l for 45 min resulted in deep /SRP: CNS depression/, recovery. Exposures to 43,000 ppm in 155 mg/l for 14-16 min resulted in deep /CNS depression/, death. /From table/
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 2982]**PEER REVIEWED**

Chinese hamsters were exposed to **ethyl acetate ...** known to be a strong inducer of aneuploidy in the yeast Saccaromyces cerevisiae. This solvent yielded negative results in the micronucleus test, whereas the vinca alkaloid vindesine used as a positive control substance proved to act as a spindle poison in mammals in vivo.
[Basler A; Mutat Res 174 (1): 11-3 (1986)]**PEER REVIEWED**

Leucopenia without change in differential or red blood cell counts was observed in rats exposed for 4 hr to increasing air concentration of ... **ethyl acetate. ...** This effect was abolished by adrenalectomy. This solvent caused leucopenia only when exposure reached the irritant level. It is discussed that stress associated with the irritative effect of chemicals can confound specific hematological effects.
[Brondeau MT et al; J Appl Toxicol 10 (2): 83-6 (1990)]**PEER REVIEWED**

In order to determine the lung disease potential of waterproofing sprays, several components of suspected sprays, as well as a commercial spray, were tested on CD-l-mice. Mice placed in inhalation chambers were exposed to aerosols containing one or more of the suspected components, including N-heptane, **ethyl-acetate,** fluororesin, silicone, and a commercial spray. An intermittent inhalation methods was used to prevent the solvents from causing anesthetic death. Mice were sacrificed 1 hour after the end of exposure. The lungs of both exposed and control mice were isolated and examined microscopically for any changes. The amounts released of the were similar. Mice exposed to the commercial and fluororesin sprays were cyanotic and depressed for 1 hour, while those exposed to the other sprays were cyanotic for only several minutes. In almost all mice exposed to the commercial spray, significant changes relative to the controls included a thickened pulmonary alveolar septa, cellular infiltration, fused and hemorrhaged alveolar walls, and diminished alveoli. Fluororesin particles were found in the alveolar space. Significantly more pronounced pathological changes were discovered in mice exposed to the fluororesin spray, relative to the commercial spray. In mice exposed to the silicone spray, significant differences were observed in alveolar collapse and hemorrhage, compared to the controls. The lungs of mice exposed to the N-heptane, **ethyl-acetate,** and fluororesin free sprays were similar to control lungs. In mice exposed to the silicon resin free spray, significant changes, relative to the commercial spray group, included alveolar collapse, hyperemia, hemorrhage and increased thickness and cellular infiltration of the septum. /It was/ concluded that **ethyl-acetate** and N-heptane contained in waterproofing sprays do not cause pulmonary disorders. Instead, fluororesin is implicated in respiratory disorders caused by such sprays.
[Yamashita M, Tanaka J; J Toxicol, Clin Toxicol 33 (6): 631-7 (1995)]**PEER REVIEWED**

The neurotoxic effects of inhaled amyl-acetate, **ethyl-acetate,** and n-butyl-acetate were investigated in mice. Male CFW-albino-mice were exposed to up to 40,000 ppm amyl-acetate, 2,000 ppm **ethyl-acetate,** or 8,000 ppm n-butyl-acetate for 20 minutes in an exposure chamber. Acute neurotoxic effects were assessed by measuring locomotor activity and functional observational battery. Similar acute behavioral effects on locomotor activity were observed in mice following **ethyl-acetate** and n-butyl-acetate exposure, with amyl-acetate inducing little neurotoxic effect. Exposure to the compounds caused changes in posture, with decreased arousal and rearing; increased central nervous system excitability, as manifested by increased tonic and clonic movements; and increased autonomic effects. Also, decreased mobility and righting reflex, and an elevated reaction to sensory stimuli were observed. Handling induced convulsions were produced in some mice following acute exposure; potency differences were observed. Significant decreases in locomotor activity were seen with exposure to **ethyl-acetate** and n-butyl-acetate at the highest concentrations tested, and minimally effective levels for activity decreasing effects were 2,000 and 8,000 ppm for **ethyl-acetate** and n-butyl-acetate, respectively. Rapid recovery was seen in mice after removal from exposure. /It was/ concluded that acute exposure to acetyl-acetate, n-butyl-acetate, and **ethyl-acetate** produces acute neurobehavioral effects which differ from the effects produced by exposure to alkylbenzenes and halogenated hydrocarbon solvents.

[Bowen SE, Balster RL; Fundam and Appl Toxicol 35 (2): 189-96 (1997)]**PEER REVIEWED**

Non-Human Toxicity Values:

LD50 Rat oral 5.6 g/kg /From table/
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 2980]**PEER REVIEWED**

LD50 Rabbit oral 4.94 g/kg /From table/
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LD50 Mouse oral 0.44 g/kg /From table/
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 2980]**PEER REVIEWED**

LD50 Guinea pig sc 3.0 g/kg /From table/
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LD50 Cat sc 3.0 g/kg /From table/
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LD50 Rat oral 11.3 ml/kg
[The Merck Index. 10th ed. Rahway, New Jersey: Merck Co., Inc., 1983. 545]**PEER REVIEWED**

LD50 Rabbit oral 4.9 g/kg
[Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984.,p. II-201]**PEER REVIEWED**

LD50 Mouse inhalation 1500 ppm/4hr
[Snyder, R. (ed.). Ethel Browning's Toxicity and Metabolism of Industrial Solvents. Second Edition. Volume 3 Alcohols and Esters. New York, NY: Elsevier, 1992. 280]**PEER REVIEWED**

LD50 Rabbit inhalation 2500 ppm/4hr
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LC50 Rat inhalation 16,000 ppm/6hr
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Volumes I,II, III. Cincinnati, OH: ACGIH, 1991. 569]**PEER REVIEWED**

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LC50 HETEROPNEUSTES FOSSILIS (COMMON INDIAN CATFISH) 212.5 PPM/96 HR /CONDITIONS OF BIOASSAY NOT SPECIFIED/
[GUPTA AB, SRIVASTAVA AK; ECOTOXICOL ENVIRON SAF 6 (2): 166-70 (1982)]**PEER REVIEWED**

LC50 Pimephales promelas (fathead minnow) 230 mg/l/96 hr (confidence limit 220-250 mg/l). Contamination of chemical in the control tanks - possibly due to volatility of the cmpd. /Conditions of bioassay not specified/
[Brooke, L.T., D.J. Call, D.T. Geiger and C.E. Northcott (eds.). Acute Toxicities of Organic Chemicals to Fathead Minnows (Pimephales Promelas). Superior, WI: Center for LakeSuperior Environmental Studies Univ. of Wisconsin Superior, 1984. 103]**PEER REVIEWED**

EC50 Pimephales promelas (fathead minnow) 220 mg/l/96 hr (confidence limit 210-240 mg/l). Contamination of chemical in the control tanks - possibly due to volatility of the cmpd. Affected fish lost equilibrium prior to death. /Conditions of bioassay not specified/
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ETHYL ACETATE

CASRN: 141-78-6

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Non-Human Toxicity Excerpts:

ANIMAL EXPERIMENTS HAVE SHOWN THAT, IN VERY HIGH CONCN, THE ESTER HAS ... /SRP: CNS DEPRESSANT/ & LETHAL EFFECTS.
[International Labour Office. Encyclopedia of Occupational Health and Safety. Volumes I and II. New York: McGraw-Hill Book Co., 1971. 477]**PEER REVIEWED**

... ANIMALS COULD WITHSTAND CONCN OF **ETHYL ACETATE** OF 2000 PPM FOR 65, 4 HR EXPOSURES WITHOUT APPARENT ILL EFFECTS AS MEASURED BY LACK OF CHANGE IN BODY WT & IN RED & WHITE BLOOD COUNTS.
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Volumes I,II, III. Cincinnati, OH: ACGIH, 1991. 569]**PEER REVIEWED**

CHRONIC, REPEATED INHALATION BY MICE 6 HR/DAY FOR 7 DAYS OF 4200-4400 PPM /& BY GUINEA PIGS OF 2000 PPM/ WAS FOUND ... TO CAUSE NO DEFINITE ... /SRP: CNS DEPRESSANT/ SYMPTOMS, BUT ... NOTED INCR IN ERYTHROCYTES WITH NO CORRESPONDING INCR IN HEMOGLOBIN, & SOME INCR IN POLYMORPHS. ... THERE WAS LOSS OF APPETITE ... NO CHANGE IN ... URINE ... .
[Snyder, R. (ed.). Ethel Browning's Toxicity and Metabolism of Industrial Solvents. Second Edition. Volume 3 Alcohols and Esters. New York, NY: Elsevier, 1992. 239]**PEER REVIEWED**

... SALIVATION, COUGHING, ... PAIN, & FOLLOWED BY DEATH OF 25% OF ANIMALS DURING PERIOD OF DEEP /SRP: CNS DEPRESSION/ ...
[Snyder, R. (ed.). Ethel Browning's Toxicity and Metabolism of Industrial Solvents. Second Edition. Volume 3 Alcohols and Esters. New York, NY: Elsevier, 1992. 239]**PEER REVIEWED**

... EXPOSURE OF RABBITS TO VAPOR AT CONCN WHICH WOULD BE SCARCELY TOLERABLE TO HUMAN BEINGS CAUSED NO CORNEAL DAMAGE DESPITE EXPOSURE FOR 8 HR A DAY, 5 DAYS A WK, FOR ... UP TO 7 WK. ONLY CONJUNCTIVAE GAVE INDICATIONS OF IRRITATION ... STD TESTING ON RABBIT EYES ... RESULTED IN RATING OF 2 ON SCALE OF 10 /10 MOST SEVERE/ ... .
[Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986. 239]**PEER REVIEWED**

WHEN **ETHYL ACETATE** WAS INJECTED INTO THE YOLK SAC OF FRESH FERTILE CHICKEN EGGS BEFORE INCUBATION IN A DOSE OF 9, 22.5, 45, OR 90 MG/EGG, THE HATCHABILITIES WERE 85, 50, 35, AND 15%, RESPECTIVELY.
[Opdyke, D.L.J. (ed.). Monographs on Fragrance Raw Materials. New York: Pergamon Press, 1979. 341]**PEER REVIEWED**

EXPOSURE OF THE FISH /COMMON INDIAN CATFISH, HETEROPNEUSTES FOSSILUS/ TO 170 PPM OF **ETHYL ACETATE** FOR 3, 6, 12, 48, & 96 HR INDUCED MARKED CHANGES IN CARBOHYDRATE METABOLISM. HEPATIC GLYCOGEN LEVELS DECLINED SIGNIFICANTLY AT 3, 48, & 96 HR, BUT THERE WAS NO MARKED ALTERATION IN MUSCLE GLYCOGEN CONTENT AT ANY OF THE EXPOSURE PERIODS. HYPERGLYCEMIA OCCURRED AT ALL TIME INTERVALS. BLOOD PYRUVATE LEVELS WERE ELEVATED AT 3, 6, 48, & 96 HR. HYPERLACTICEMIA RESULTED AT 3 & 96 HR, BUT HYPOLACTICEMIA OCCURRED AT 6 & 12 HR. IMPAIRMENT OF CARBOHYDRATE METABOLISM MIGHT BE RESPONSIBLE FOR THE TOXIC ACTION OF **ETHYL ACETATE.**
[GUPTA AB, SRIVASTAVA AK; ECOTOXICOL ENVIRON SAF 6 (2): 166-70 (1982)]**PEER REVIEWED**

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[Bowen SE, Balster RL; Fundam and Appl Toxicol 35 (2): 189-96

(1997)]**PEER REVIEWED**

ETHYL ACETATE

CASRN: 141-78-6

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Non-Human Toxicity Values:

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[Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984.,p. II-201]**PEER REVIEWED**

LD50 Mouse inhalation 1500 ppm/4hr

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LC50 Rat inhalation 16,000 ppm/6hr
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ETHYL ACETATE

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Ecotoxicity Values:

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[GUPTA AB, SRIVASTAVA AK; ECOTOXICOL ENVIRON SAF 6 (2): 166-70 (1982)]**PEER REVIEWED**

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ETHYL ACETATE

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Metabolism/Pharmacokinetics:

Metabolism/Metabolites:

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[Snyder, R. (ed.). Ethel Browning's Toxicity and Metabolism of Industrial Solvents. Second Edition. Volume 3 Alcohols and Esters. New York, NY: Elsevier, 1992. 237]**PEER REVIEWED**

AT HIGHER LEVELS, THE RATE OF HYDROLYSIS OF **ETHYL ACETATE /**IN RATS/ APPEARED TO EXCEED ETHANOL OXIDATION, LEADING TO ITS (ETHANOL'S) ACCUMULATION IN THE VASCULAR SYSTEM. ALSO, WHEN IT (**ETHYL ACETATE)** WAS INJECTED IP AT 1.6 G/KG, HYDROLYSIS TO ACETIC ACID AND ETHANOL OCCURRED RAPIDLY.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994.,p. 2983-4]**PEER REVIEWED**

Absorption, Distribution & Excretion:

Ethyl acetate may cause adverse health effects following exposure via inhalation, ingestion or dermal contact. The primary route of absorption responsible for the toxicity of **ethyl acetate** is inhalation.
[Ryan, R.P., C.E. Terry (eds.). Toxicology Desk Reference 4th ed. Volumes 1-3. Taylor & Francis, washington, D.C. 1997. 1253]**PEER REVIEWED**

Biological Half-Life:

... THE BIOLOGICAL HALF-LIFE VALUES OF THE CONVERSION /OF **ETHYL ACETATE** TO ETHANOL/ IN VITRO AND IN VIVO WERE FOUND TO BE 65 AND 5-10 MIN RESPECTIVELY.
[The Chemical Society. Foreign Compound Metabolism in Mammals. Volume 4: A Review of the Literature Published during 1974 and 1975. London: The Chemical Society, 1977. 233]**PEER REVIEWED**

Interactions:

ETHYL ACETATE IN COMBINATION WITH TOLUENE APPEARED TO PRODUCE A MIXTURE OF LOWER TOXICITY THAN THAT OF EITHER COMPOUND ALONE. MIXING OF **ETHYL ACETATE** WITH PROPYLENE OXIDE, PROPYLENE GLYCOL, OR FORMALIN APPEARS TO DECR ITS LD50 VALUE, BUT ITS TOXICITY INCREASES IN COMBINATION WITH MORPHOLINE, ETHYLENE GLYCOL, OR ETHYL ALCOHOL.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New

York, NY: John Wiley & Sons Inc., 1993-1994. 2984]**PEER REVIEWED**

ETHYL ACETATE

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For other data, click on the Table of Contents

Biological Half-Life:

... THE BIOLOGICAL HALF-LIFE VALUES OF THE CONVERSION /OF **ETHYL ACETATE** TO ETHANOL/ IN VITRO AND IN VIVO WERE FOUND TO BE 65 AND 5-10 MIN RESPECTIVELY. [The Chemical Society. Foreign Compound Metabolism in Mammals. Volume 4: A Review of the Literature Published during 1974 and 1975. London: The Chemical Society, 1977. 233]**PEER REVIEWED**

ETHYL ACETATE

CASRN: 141-78-6

For other data, click on the Table of Contents

Interactions:

ETHYL ACETATE IN COMBINATION WITH TOLUENE APPEARED TO PRODUCE A MIXTURE OF LOWER TOXICITY THAN THAT OF EITHER COMPOUND ALONE. MIXING OF **ETHYL ACETATE** WITH PROPYLENE OXIDE, PROPYLENE GLYCOL, OR FORMALIN APPEARS TO DECR ITS LD50 VALUE, BUT ITS TOXICITY INCREASES IN COMBINATION WITH MORPHOLINE, ETHYLENE GLYCOL, OR ETHYL ALCOHOL.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 2984]**PEER REVIEWED**

ETHYL ACETATE

CASRN: 141-78-6

For other data, click on the Table of Contents

Pharmacology:

Therapeutic Uses:

Anti-Arrhythmia Agents

[National Library of Medicine's Medical Subject Headings online file (MeSH, 1999)]**QC REVIEWED**

... IT HAS BEEN USED INTERNALLY IN A DOSE OF 1 TO 2 CC AS CARMINATIVE & ANTISPASMODIC, ALSO EXTERNALLY AS COUNTERIRRITANT ... .

[Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986. 412]**PEER REVIEWED**

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ETHYL ACETATE IN COMBINATION WITH TOLUENE APPEARED TO PRODUCE A MIXTURE OF LOWER TOXICITY THAN THAT OF EITHER COMPOUND ALONE. MIXING OF **ETHYL ACETATE** WITH PROPYLENE OXIDE, PROPYLENE GLYCOL, OR FORMALIN APPEARS TO DECR ITS LD50 VALUE, BUT ITS TOXICITY INCREASES IN COMBINATION WITH MORPHOLINE, ETHYLENE GLYCOL, OR ETHYL ALCOHOL.

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ETHYL ACETATE

CASRN: 141-78-6

For other data, click on the Table of Contents

Environmental Fate & Exposure:

Environmental Fate/Exposure Summary:

Ethyl acetate's production and use as a pharmaceutic aid, in artificial fruit essences, and as a solvent may result in its release to the environment through various waste streams. If released to air, a vapor pressure of 93 mm Hg at 25 deg C indicates **ethyl acetate** will exist solely as a vapor in the ambient atmosphere. Vapor-phase **ethyl acetate** will be degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals; the half-life for this reaction in air is estimated to be 9.4 days. If released to soil, **ethyl acetate** is expected to have high mobility based upon an estimated Koc of 59. Volatilization from moist soil surfaces is expected to occur based upon a Henry's Law constant of 1.34X10-4 atm-cu m/mole. **Ethyl acetate's** vapor pressure indicates the potential for volatilization from dry soil surfaces exists. Biodegradation is expected to be an important process in both soil and water, based upon **ethyl acetate's** biodegradation in aqueous screening studies. 93% biodegradation was observed in a complete mix continuous-flow activated sludge system. 26.6 and 57.1% of **ethyl acetate'**s theoretical BOD was reached in 5 days using the standard dilution method and seawater dilution method, respectively. If released into water, **ethyl acetate** is not expected to adsorb to suspended solids and sediment in water based on the estimated Koc. Volatilization from water surfaces is expected to be an important fate process based on **ethyl acetate's** Henry's Law constant. Estimated volatilization half-lives for a model river and model lake are 8.9 hours and 5.6 days, respectively. An estimated BCF of 3.2 suggests the potential for bioconcentration in aquatic organisms is low. **Ethyl acetate's** hydrolysis half-life at 25 deg C and pH 7 is 2.0 years. Occupational exposure to **ethyl acetate** may occur through inhalation and dermal contact with this compound at workplaces where **ethyl acetate** is produced or used or where adhesives, thinners, degreasers, paints, inks, and dome reagents are used. The general population may be exposed to **ethyl acetate** via inhalation of ambient air, ingestion of food and drinking water, or dermal contact with consumer products containing this compound. (SRC)
PEER REVIEWED

Probable Routes of Human Exposure:

NIOSH (NOES Survey 1981-1983) has statistically estimated that 375,906 workers (87,691 of these are female) are potentially exposed to **ethyl acetate** in the US(1). Occupational exposure to **ethyl acetate** may occur through inhalation and dermal contact with this compound at workplaces where **ethyl acetate** is produced or used(SRC). **Ethyl acetate** was identified (relative abundance) in air samples collected where printing pastes (66%) and paints (30%) were used, in car repair shops (45%), and in various other industries (57%) in Belgium(2). Mean concentrations of **ethyl acetate** in air during parquet work in Finland were 119 ppm during installation with resin adhesives; 319 ppm during puttying; 72 ppm during sanding after puttying; 413 ppm during undercoat varnishing (nitrocellulose); 64 ppm during urea-formaldehyde varnishing; and 1 ppm during work with water-based varnishes(3). It was also detected in air during the use of contact adhesives at mean concentrations of 14 ppm during repair of a textile carpet (dispersion and contact adhesives); 83 ppm during repair of a textile carpet (contact adhesives only); 29 ppm during beading of textile carpets (contact adhesives only); and 71 ppm during repair of bathroom floor mats (dispersion and contact adhesives)(3). **Ethyl acetate** was detected in 36%

of all air samples, at a mean concentration of 11 ppm, collected from Finnish furniture factories from 1975 to 1984(4). Breathing zone samples collected during spray painting contained **ethyl acetate** at a geometric mean concentration of 9.51 ppm(5). It was detected in the air of one auto paint shop at a concentration of 10.5 mg/cu m(6). **Ethyl acetate** was identified in 12% of 275 products (including thinners, degreasers, paints, inks, and dome reagents) used in workplaces in various industries(7). **Ethyl acetate** was identified in the breathing zone of shoe factory workers(8). **Ethyl acetate** was detected in the ambient air of shoe factory in Italy in Nov 1991 at median concentrations of 10 and 7 mg/cu m(9).
[(1) NIOSH; National Occupational Exposure Survey (NOES) (1983) (2) Veulemans H et al; Am Indust Hyg Assoc J 48: 671-7 (1987) (3) Riala REE, Riihimaki HA; Appl Occup Environ Hyg 6: 301-8 (1991) (4) Priha E; Ann Occup Hyg 30: 289-94 (1986) (5) Myer HE et al; Am Ind Hyg Assoc J 54: 663-70 (1993) (6) Medinilla J, Espigares M; Ann Occup Hyg 32: 509-13 (1988) (7) Lehman E et al; pp. 31-41 in Safety and Health ASP Org Sol Expos Finland April 1985, Riihimaki V, Ulfvarson U, eds NY,NY: Alan R Liss Inc (1986) (8) Ahonen I, Schimberg RW; Br J Ind Med 45: 133-6 (1988) (9) Mutti A et al; Int Arch Occup Environ Health 65: S171-6 (1993)]**PEER REVIEWED**

The general population may be exposed to **ethyl acetate** via inhalation of ambient air, ingestion of food and drinking water, and dermal contact with consumer products containing **ethyl acetate. (**SRC)
PEER REVIEWED

Body Burden:

Mother's milk from 4 urban areas in the USA, 1 of 8 samples positive(1). 7 out of 12 breath samples collected from nine volunteers in Bayonne and Elizabeth, NJ between July and Dec 1980 contained **ethyl acetate** at unreported concentrations(2). **Ethyl acetate** was identified as a component in 13.7% of expired air samples from 54 volunteers in the Chicago area at a geometric mean concentration of 0.447 ng/l(3). **Ethyl acetate** was detected in expired air samples from 5 of 8 male volunteers at levels ranging from 0.30 to 190.0 ug/hr(4).
[(1) Pellizzari ED et al; Environ Sci Technol 16: 781-5 (1982) (2) Wallace LA et al; Environ Res 35: 293-319 (1984) (3) Krotoszynski BK et al; J Anal Toxicol 3: 225-34 (1979) (4) Conkle JP et al; Arch Environ Health 30: 290-5 (1975)]**PEER REVIEWED**

Natural Pollution Sources:

Ethyl acetate is a natural product of fermentation(1,2). Natural sources of **ethyl acetate** include animal waste, plant volatiles, and microbes(1).
[(1) Graedel TE; Chemical Compounds in the Atmosphere. NY,NY: Academic Press pp. 223-34 (1978) (2) Reed G; Kirk-Othmer Encycl Chem Tech; 3rd ed NY,NY: Wiley Interscience 24: 789 (1983)]**PEER REVIEWED**

Artificial Pollution Sources:

Ethyl acetate's production and use as a pharmaceutic aid (flavor); in artificial fruit essences; as a solvent; in the manufacture of smokeless powder, artificial leather, and photographic films and plates; and in cleaning textiles(1) may result in its release to the environment through various waste

streams(SRC).
[(1) Budavari S; The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. 12th ed. Whitehouse Station, NJ: Merck and Co Inc p 641 (1996)]**PEER REVIEWED**

Environmental Fate:

TERRESTRIAL FATE: Based on a classification scheme(1), an estimated Koc value of 59(SRC), determined from a log Kow of 0.73(2) and a regression-derived equation(3), indicates that **ethyl acetate** is expected to have high mobility in soil(SRC). Volatilization of **ethyl acetate** from moist soil surfaces is expected to be important(SRC) given a Henry's Law constant of 1.34X10-4 atm-cu m/mole(4). The potential for volatilization of **ethyl acetate** from dry soil surfaces may exist(SRC) based on a vapor pressure of 93 mm Hg(5). **Ethyl acetate** may biodegrade in soil(SRC), based upon its biodegradation in aqueous screening studies(6,7).
[(1) Swann RL et al; Res Rev 85: 23 (1983) (2) Hansch C et al; Exploring QSAR. Hydrophobic, Electronic, and Steric Constants. ACS Professional Reference Book. Heller SR (consult ed) Washington,DC: Amer Chem Soc p. 9 (1995) (3) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington,DC: Amer Chem Soc pp. 4-9 (1990) (4) Butler JAV, Tamchandani CN; J Chem Soc: 952-5 (1935) (5) Daubert TE, Danner RP; Physical and Thermodynamic Properties of Pure Chemicals: Data Compilation. Design Inst Phys Prop Data, Amer Inst Chem Eng., NY,NY: Hemisphere Pub Corp, Vol 2 (1991) (6) Takemoto S et al; Suishitsu Odaka Kenkyu 4: 80-90 (1981) (7) Kincannon DF et al; J Water Pollut Control Fed 55: 157-63 (1983)]**PEER REVIEWED**

AQUATIC FATE: Based on a classification scheme(1), an estimated Koc value of 59(SRC), determined from a log Kow of 0.73(2) and a regression-derived equation(3), indicates that **ethyl acetate** is not expected to adsorb to suspended solids and sediment in water(SRC). **Ethyl acetate** is expected to volatilize from water surfaces(3,SRC) based on a Henry's Law constant of 1.34X10-4 atm-cu m/mole(4). Estimated volatilization half-lives for a model river and model lake are 8.9 hours and 5.6 days, respectively(3,SRC). According to a classification scheme(5), an estimated BCF of 3.2(3,SRC), from the log Kow(2), suggests the potential for bioconcentration in aquatic organisms is low(SRC). Simple esters are resistant to hydrolysis; **ethyl acetate's** hydrolysis half-life at 25 deg C and pH 7 is 2.0 years(6). Biodegradation is expected to be an important process in aquatic systems(SRC), based upon aqueous screening studies(7,8). **Ethyl acetate** reached 26.6 and 57.1% of its theoretical BOD in 5 days using the standard dilution method and seawater dilution method, respectively(7). 99.9% removal of **ethyl acetate** was observed in a complete mix continuous-flow activated sludge system; 93% of this removal was attributed to biodegradation(8). 94% of theoretical methane production was observed after incubation in sediment and groundwater collected from the methanogenic portion of an anoxic aquifer polluted by municipal landfill leachate(9).
[(1) Swann RL et al; Res Rev 85: 23 (1983) (2) Hansch C et al; Exploring QSAR. Hydrophobic, Electronic, and Steric Constants. ACS Professional Reference Book. Heller SR (consult ed) Washington,DC: Amer Chem Soc p 9 (1995) (3) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington,DC: Amer Chem Soc pp. 4-9, 5-4, 5-10, 15-1 to 15-29 (1990) (4) Butler JAV, Tamchandani CN; J Chem

Soc: 952-5 (1935) (5) Franke C et al; Chemosphere 29: 1501-14 (1994) (6) Mabey WR et al; J Phys Chem Ref Data Vol 7, No. 2 p. 411 (1978) (7) Takemoto S et al; Suishitsu Odaka Kenkyu 4: 80-90 (1981) (8) Kincannon DF et al; J Water Pollut Control Fed 55: 157-63 (1983) (9) Sulfita JM, Mormile MR; Environ Sci Technol 27: 976-8 (1993)]**PEER REVIEWED**

ATMOSPHERIC FATE: According to a model of gas/particle partitioning of semivolatile organic compounds in the atmosphere(1), **ethyl acetate,** which has a vapor pressure of 93 mm Hg at 25 deg C(2), is expected to exist solely as a vapor in the ambient atmosphere. Vapor-phase **ethyl acetate** is degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals(SRC); the half-life for this reaction in air is estimated to be 10 days(3,SRC).
[(1) Bidleman TF; Environ Sci Technol 22: 361-367 (1988) (2) Daubert TE, Danner RP; Physical and Thermodynamic Properties of Pure Chemicals: Data Compilation. Design Inst Phys Prop Data, Amer Inst Chem Eng., NY,NY: Hemisphere Pub Corp, Vol 2 (1991) (3) Atkinson R; J Phys Chem Ref Data Monograph 1 p. 166 (1989)]**PEER REVIEWED**

Environmental Biodegradation:

ANAEROBIC: **Ethyl acetate** has been demonstrated to be amenable to anaerobic biodegradation(1). It was mineralized (>75% of theoretical methane production) in 10% sludge from a secondary digester within 8 weeks(2). 96% utilization occurred in an anaerobic reactor with a 20 day retention time(3). **Ethyl acetate,** at a concentration of 1000 mg/l, was readily degraded in batch reactors containing anaerobic solids from an industrial anaerobic digester with some exposure to **ethyl acetate(**4). 100% loss of **ethyl acetate** was observed in aquifer slurries amended with sulfate and nitrate following 244 days and 85 days incubation, respectively(5). 94% of theoretical methane production was observed after incubation in sediment and groundwater collected from the methanogenic portion of an anoxic aquifer polluted by municipal landfill leachate(6).
[(1) Speece RE; Environ Sci Tech 17: 416A-27A (1983) (2) Shelton DR, Tiedje JM; Appl Environ Microbiol 47: 850-7 (1984) (3) Chou WL et al; Biotech Bioeng Symp 8: 391-414 (1979) (4) Schwartz LJ; Appl Biochem Biotehcnol 28/29: 297-305 (1991) (5) Mormile MR et al; Environ Sci Technol 28: 1727-32 (1994) (6) Sulfita JM, Mormile MR; Environ Sci Technol 27: 976-8 (1993)]**PEER REVIEWED**

A review concluded that **ethyl acetate** is easily removed by biological treatment(1). Reported 5 day BOD values using a sewage inoculum range from 36-68% of theoretical(2-5) with the value being somewhat reduced in salt water(2). One investigator reported that **ethyl acetate** was completely degraded in 20 hr using activated sludge(6). In a bench-scale continuous-flow activated sludge reactor with an 8 hour retention time, 99.9% removal (including 17% volatilization loss) was obtained, with 80% of the theoretical BOD(7). **Ethyl acetate** was 90% biooxidized in a 20-day BOD test using a filtered raw sewage seed; it was biooxidized 77% in a 28-day OECD closed-bottle test(8). A screening procedure that was systematically applied to a large number of organic chemicals ranked **ethyl acetate** as being completely biodegraded in a short time by general microorganisms(9). After a 5 hr lag, 43 to 53% of theoretical BOD was obtained in 50 to 70 hr(9). In screening tests, **ethyl acetate,** present at a concentration of 5 ppm, reached 26.6 and 57.1% of its theoretical BOD in 5 days using the standard

dilution method and seawater dilution method, respectively(10). 99.9% removal of **ethyl acetate** was observed in a complete mix continuous-flow activated sludge system; 93% of this removal was attributed to biodegradation(11).
[(1) Thom NS, Agg AR; Proc Roy Soc London B 189: 347-57 (1975) (2) Price KS et al; J Water Pollut Control Fed 46: 63-77 (1974) (3) Ettinger MB; Ind Eng Chem 48: 256-9 (1956) (4) Young RHF et al; J Water Pollut Control Fed 40: 354-68 (1968) (5) Heukelekian H, Rand MC; J Water Pollut Control Assoc 29: 1040-53 (1955) (6) Slave T et al; Rev Chim 25: 666-70 (1974) (7) Stover EL, Kincannon DF; J Water Pollut Control Fed 55: 97-109 (1983) (8) Waggy GT et al; Environ Toxicol Chem 13: 1277-80 (1994) (9) Urano K, Kato Z; J Haz Mat 13: 135-45, 147-59 (1986) (10) Takemoto S et al; Suishitsu Odaka Kenkyu 4: 80-90 (1981) (11) Kincannon DF et al; J Water Pollut Control Fed 55: 157-63 (1983)]**PEER REVIEWED**

Environmental Abiotic Degradation:

The rate constant for the vapor-phase reaction of **ethyl acetate** with photochemically-produced hydroxyl radicals is 1.6X10-12 cu cm/molecule-sec at 25 deg C(1). This corresponds to an atmospheric half-life of about 10 days at an atmospheric concentration of 5X10+5 hydroxyl radicals per cu cm(1,SRC). The observed rate constant for the vapor-phase reaction of **ethyl acetate** with nitrate radicals is 1.4X10-17 cu cm/molecule-sec(2). This corresponds to an atmospheric half-life of about 16 years at an average nighttime nitrate radical concentration of 2X10+8 molecules/cu cm (nitrate radicals are unstable in sunlight)(3,SRC). The rate constant for the reaction of **ethyl acetate** with hydroxyl radicals in aqueous solution is 4.0X10+8 L/mol sec(4). This corresponds to a half-life of about 5.5 years(SRC) at an average aqueous hydroxyl radical concentration of 1X10-17 mol/l(5). Simple esters are resistant to hydrolysis; **ethyl acetate's** hydrolysis half-life at 25 deg C and pH 7 is 2.0 years(6).
[(1) Atkinson R; J Phys Chem Ref Data Monograph 1 p. 166 (1989) (2) Atkinson R; J Phys Chem Ref Data Monograph p. 213 (1994) (3) GEMS; Graphical Exposure Modeling System. FAP. Fate of Atmos Pollut (1986) (4) Buxton GV et al; J Phys Chem Ref Data 17: 513-882 (1988) (5) Mill T et al; Science 207: 886-7 (1980) (6) Mabey WR et al; J Phys Chem Ref Data Vol 7, No. 2 p. 411 (1978)]**PEER REVIEWED**

Environmental Bioconcentration:

An estimated BCF of 3.2 was calculated for **ethyl acetate(**SRC), using a log Kow of 0.73(1) and a regression-derived equation(2). According to a classification scheme(3), this BCF suggests the potential for bioconcentration in aquatic organisms is low(SRC).
[(1) Hansch C et al; Exploring QSAR. Hydrophobic, Electronic, and Steric Constants. ACS Prof Ref Book. Heller SR (consult ed) Washington,DC: Amer Chem Soc p. 9 (1995) (2) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington DC: Amer Chem Soc pp. 5-4, 5-10 (1990) (3) Franke C et al; Chemosphere 29: 1501-14 (1994)]**PEER REVIEWED**

Soil Adsorption/Mobility:

The Koc of **ethyl acetate** is estimated as 59(SRC), using a log Kow of 0.73(1) and a regression-derived equation(2,SRC). According to a classification scheme(3), this estimated Koc value suggests that **ethyl acetate** is expected to have high mobility in soil(SRC).
[(1) Hansch C et al; Exploring QSAR. Hydrophobic, Electronic, and Steric Constants. ACS Prof Ref Book. Heller SR (consult ed) Washington,DC: Amer Chem Soc p. 9 (1995) (2) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington,DC: Amer Chem Soc pp. 4-9 (1990) (3) Swann RL et al; Res Rev 85: 23 (1983)]**PEER REVIEWED**

Volatilization from Water/Soil:

The Henry's Law constant for **ethyl acetate** is 1.34X10-4 atm-cu m/mole(1). This Henry's Law constant indicates that **ethyl acetate** is expected to volatilize from water surfaces(2,SRC). Based on this Henry's Law constant, the estimated volatilization half-life from a model river (1 m deep, flowing 1 m/sec, wind velocity of 3 m/sec) is estimated as 8.9 hours(2,SRC). The estimated volatilization half-life from a model lake (1 m deep, flowing 0.05 m/sec, wind velocity of 0.5 m/sec) is estimated as 5.6 days(2,SRC). **Ethyl acetate's** Henry's Law constant(1) indicates that volatilization from moist soil surfaces may occur(SRC). The potential for volatilization of **ethyl acetate** from dry soil surfaces may exist(SRC) based on a vapor pressure of 93 mm Hg(3). 7% of the 99.9% removal observed in a continuous flow activated sludge system was attributed to stripping(4).
[(1) Butler JAV, Tamchandani CN; J Chem Soc: 952-5 (1935) (2) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington,DC: Amer Chem Soc pp. 15-1 to 15-29 (1990) (3) Daubert TE, Danner RP; Physical and Thermodynamic Properties of Pure Chemicals: Data Compilation. Design Inst Phys Prop Data, Amer Inst Chem Eng., NY,NY: Hemisphere Pub Corp, Vol 2 (1991) (4) Kincannon DF et al; J Water Pollut Control Fed 55: 157-63 (1983)]**PEER REVIEWED**

Environmental Water Concentrations:

DRINKING WATER: **Ethyl acetate** was detected, not quantified in 3 New Orleans drinking water plants(1). It was detected in drinking water, no levels given(2). **Ethyl acetate** was identified in commercially bottled Artesian water(3).
[(1) Keith LH et al; pp. 329-73 in Identification and Analysis of Organic Pollutants in Water Keith LH ed Ann Arbor Press, Ann Arbor MI (1976) (2) Kool HJ et al; Crit Rev Environ Control 12: 307-57 (1982) (3) Dowty BJ et al; Environ Sci Technol 9: 762-5 (1975)]**PEER REVIEWED**

GROUNDWATER: It was not detected in an aquifer polluted by a paint factory even though **ethyl acetate** was stored in buried tanks that leaked(1).
[(1) Botta D et al; Comm Eur Com Eur 8518 (Anal Org Micropollut Water): 261-75 (1984)]**PEER REVIEWED**

SURFACE WATER: 14 heavily industrialized river basins in USA (204 sites)-only 1 site (Delaware River Basin) positive-1 ppb(1). Hayashida River in Tatsumo City, Japan (site of leather industry) 585 ppb(2). **Ethyl acetate** was identified in water samples from the brook, Rickenbach East, Switzerland,

which receives discharges from a paint factory(3).
[(1) Ewing BB et al; Monitoring to Detect Previously Unrecognized Pollutants in Surface Waters p. 75 USEPA-560/6-77-015 (1977) (2) Yasuhara A et al; Environ Sci Technol 15: 570-3 (1981) (3) Juettner F; Wat Sci Tech 25: 155-64 (1992)]**PEER REVIEWED**

Effluent Concentrations:

Effluent gas from the metal painting factory and from the lumber painting factory contained **ethyl acetate.**
[Yasuhara A et al; Chemosphere 13 (3): 469-82 (1984)]**PEER REVIEWED**

Ethyl acetate was detected, not quantified in oil refinery final effluent(1) and effluent from sewage treatment plants(2). **Ethyl acetate** has been detected in U.S. municipal landfill leachate at concentrations ranging from 42 to 290 g/l(3). **Ethyl acetate** was identified, but not quantified, in hazardous waste samples from a Midwest remedial action site(4). **Ethyl acetate** was detected, but not quantified, in a grab sample of oil refinery final effluent from a refinery in Lockport, IL(5). **Ethyl acetate** was identified as a volatile organic compound in a composite waste sample obtained from a barge which dumped its waste on Feb 9, 1978 at the Puerto Rico dumpsite(6). **Ethyl acetate** was identified in flue gas from a waste incineration plant in Germany(7).
[(1) Ellis DD et al; Arch Environ Contam Toxicol 11: 373-82 (1982) (2) Shackelford WM, Keith LH; Frequency of Organic Compounds Identified in Water USEPA-600/4-76-062 (1976) (3) Roy WR; Contam Groundwaters, Adriano DC et al eds, Sci Rev: Northwood, UK 411-46 (1994) (4) Puskar MA et al; Environ Sci Technol 21: 90-6 (1987) (5) Ellis DD et al; Arch Environ Contam Toxicol 11: 373-82 (1982) (6) Brooks JM et al; Wastes Ocean, Vol 1, Duedall, IW ed, NY,NY: Wiley pp. 171-98 (1983) (7) Jay K, Stieglitz L; Chemosphere 30: 1249-60 (1995)]**PEER REVIEWED**

Atmospheric Concentrations:

URBAN/SUBURBAN: **Ethyl acetate** was detected, not quantified in Leningrad, USSR(1). Average concentrations of **ethyl acetate** in urban air samples collected from four different sites in Stockholm ranged from 0.27 to 2.64 ppb; the average concentration at a site 12 km outside Stockholm was 0.23 ppb(2). It was identified in ambient air from Pasadena, TX, Houston, TX, and Glendora, CA(3).
SOURCE AREAS: It was detected in ambient air surrounding Kin Buc waste disposal site (4 sites) 0, trace, 4.1, 230 ug/cu m(4). **Ethyl acetate** was detected in ambient air near a furnace used for incinerating paint wastes at a concentration of 0.7 ppbv(5).
[(1) Ioffe BV et al; J Chromatogr 142: 787-95 (1977) (2) Jonsson AE et al; Environ Int 11: 383-92 (1985) (3) Pellizarri ED; Development of Analytical Techniques for Measuring Ambient Atmospheric Carcinogenic Vapors, EPA-600/2-75-076 (1975) (4) Pellizarri ED; Environ Sci Technol 16: 781-5 (1982) (5) Kelly TJ et al; Environ Sci Technol 27: 1146-53 (1993)]**PEER REVIEWED**

OTHER: 5 out of 8 personal air samples collected from volunteers in Bayonne and Elizabeth, NJ between July and Dec 1980 contained **ethyl acetate** at unreported concentrations(1). **Ethyl acetate** was identified in air at a forest site in the Eggegebirge in North Rhine-Westfalia, West Germany(2).

INDOOR: **Ethyl acetate** was detected in air samples taken from preschools in Stockholm(3). **Ethyl acetate** was detected in indoor air samples from Northern Italy at concentrations of 9 and 26 ug/cu m(4). It was detected in indoor air collected in a machine shop and a new office area at concentrations of 1.4 and 21.8 ppbv, respectively(5). **Ethyl acetate** was detected in the indoor air of 12 out of 12 Canadian homes in Nov and Dec 1986 at concentrations ranging from 3 to 13 ug/cu m, average 8.9 ug/cu m; indoor air concentrations in 6 Canadian homes in Feb and March 1987 ranged from 7 to 494 ug/cu m, average 153 ug/cu m (outdoor air average concentration 10 ug/cu m)(6). **Ethyl acetate** was detected in indoor air of new and recently renovated buildings in Switzerland at a maximum concentration of 1052 ug/cu m(7). It was detected in at least one indoor air sample from 17 locations from two Stockholm preschools(8).
[(1) Wallace LA et al; Environ Res 35: 293-319 (1984) (2) Helmig D et al; Chemosphere 19: 1399-1412 (1989) (3) Noma E et al; Atmos Environ 22: 451-60 (1988) (4) DeBortoli M et al; Environ Int 12: 343-50 (1986) (5) Kelly TJ et al; Environ Sci Technol 27: 1146-53 (1993) (6) Chan CC et al; J Air Waste Manage Assoc 40: 62-7 (1990) (7) Rothweiler H et al; Atmos Environ 26A: 2219-25 (1992) (8) Noma E et al; Aimos Environ 22: 451-60 (1988)]**PEER REVIEWED**

Food Survey Values:

Ethyl acetate forms from the reaction of acetyl coenzyme A with ethanol, and its formation depends greatly on temperature. Maximum formation occurs at 20-25 deg C. Therefore, top fermented beers contain higher amounts of this ester.
[Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984.,p. V24 789 (1984)]**PEER REVIEWED**

Ethyl acetate is found in USA lager beer, 25 to 50 ppm(1). It is a component of Orleans vinegar(2) and artificial grape flavoring(3). **Ethyl acetate** was identified as a volatile component of roasted filberts(4), fried bacon(5), Beaufort cheese(6), blue cheese(7), Idaho Russet Burbank baked potatoes(8), and the edible Korean chamchwi plant(9). Korean salt-fermented anchovy, big-eyed herring, hair tail viscera and shrimp pastes contained **ethyl acetate** at mean concentrations of 3490, 1660, 2340, and 3750 ng/g, respectively(10). **Ethyl acetate** was detected in beer at a concentration of 8 ppm(11). **Ethyl acetate** was identified as a volatile compound in kiwi fruit, comprising 3.9, 4.7, and 1.6% of the components in mature, ripe, and very ripe fruit, respectively(12). It was also identified as a volatile component of pineapple guava at a concentration of 0.11 ug/g(13). Fresh grapefruit juice contained 1.65 ppm **ethyl acetate(**14). **Ethyl acetate** was identified in mature and overripe guava fruits at concentrations of 614.1 and 8884.2 ug/kg, respectively(15). It was identified as a volatile flavor component of the strawberry variety Sivetta and in Golden Delicious apples(16).
[(1) Reed G; Kirk-Othmer Encycl Chem Tech 3rd ed. NY,NY: Wiley Interscience 24: 789 (1983) (2) Webb AD; Kirk-Othmer Encycl Chem Tech 3rd ed. NY,NY: Wiley Interscience 23: 757 (1983) (3) Jones MB; Kirk-Othmer Encycl Chem Tech 3rd ed. NY,NY: Wiley Interscience 4: 712 (1978) (4) Kinlin TE et al; J Agric Food Chem 20: 1021-8 (1972) (5) Ho CT et al; J Agric Food Chem 31: 336-42 (1983) (6) Dumont JP, Adda J; J Agric Food Chem 26: 364-7 (1978) (7) Day EA, Anderson DF; J Agric Food Chem 13: 2-4 (1965) (8) Coleman EC et al; J Agric Food Chem 29: 42-8 (1981) (9) Chung TY et al; J Agric Food Chem 41: 1693-7 (1993) (10)

Cha YJ, Cadwallader KR; J Food Sci 60: 19-24 (1995) (11) Hashimoto H, Kuroiwa YJ; J Inst Brewing 72: 151-62 (1966) (12) Bartley JP, Schwede AM; J Agric Food Chem 37: 1023-5 (1989) (13) Binder RG, Flath RA; J Agric Food Chem 37: 734-6 (1989) (14) Cadwallader KR, Xu Y; J Agric Food Chem 42: 782-4 (1994) (15) Chyau CC et al; J Agric Food Chem 40: 846-9 (1992) (16) Dirinck P et al; Analysis of Volatiles, Berlin,Germany: Walter Degruyter and Co 381-400 (1984)]**PEER REVIEWED**

Ethyl acetate was identified as a volatile component of duck meat, duck fat, Cantonese style roasted duck, and Cantonese style roasted duck gravy at concentrations of <0.05, 2.43, 23.94, and <0.05 ppb wet weight, respectively(1). It was identified as a volatile compound in fried chicken flavor(2), nectarines(3), Concord grape essence(4), three Conn Creek wines(5), Sukiyaki(6), bananas(7), and floured Chickpea seed(8). **Ethyl acetate** was detected in fresh hand-squeezed (mechanically) unpasteurized orange juice from five different cultivars and one hybrid at concentrations of, ppm: 0.28 (0.15 to 0.25) in Valencia oranges; 0.17 to 0.23 (0.15) in Pineapple oranges; 0.12 to 0.13 in Hamlin oranges; 0.77 in Florida navel oranges; 0.17 in California navel oranges; 0.28 in Pera oranges; and 0.12 (0.082) in Ambersweet oranges(9). Large amounts of **ethyl acetate** were detected in headspace from Bisbee Delicious apples at the earliest harvests(10).
[(1) Wu CM, Liou SE; J Agric Food Chem 40: 838-41 (1992) (2) Tang J et al; J Agric Food Chem 31: 1287-92 (1983) (3) Takeoka GR et al; J Agric Food Chem 36: 553-60 (1988) (4) Stevens KL et al; J Food Sci 30: 1006-7 (1965) (5) Shimoda M et al; J Agric Food Chem 41: 1664-66 (1993) (6) Shibamoto T et al; J Agric Food Chem 29: 57-63 (1981) (7) Macku C, Jennings WG; J Agric Food Chem 35: 845-8 (1987) (8) Rembold H et al; J Agric Food Chem 37: 659-62 (1989) (9) Moshonas MG, Shaw PE; J Agric Food Chem 42: 1525-8 (1994) (10) Mattheis JP et al; J Agric Food Chem 39: 1902-6 (1991)]**PEER REVIEWED**

Plant Concentrations:

Ethyl acetate was identified as a volatile component of kiwi fruit flowers(1). Volatile emissions from Scots pine were found to contain **ethyl acetate(**2).
[(1) Tatsuka K et al; J Agric Food Chem 38: 2176-80 (1990) (2) Singh HB, Zimmerman PB; Adv Environ Sci Technol 24: 177-235 (1992)]**PEER REVIEWED**

Fish/Seafood Concentrations:

Ethyl acetate was identified in a sample of mussel collected from the Oarai Coast in Ibaraki, Japan on July 31, 1985 at a concentration of 97.1 ug/g(1).
[(1) Yashuara A, Morita M; Chemosphere 16: 2559-65 (1987)]**PEER REVIEWED**

Milk Concentrations:

Mother's milk from 4 urban areas in the USA, 1 of 8 samples positive(1).
[(1) Pellizarri ED et al; Environ Sci Technol 16: 781-5 (1982)]**PEER

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Other Environmental Concentrations:

Nail polish remover typically contains 40 wt% **ethyl acetate(**1,2). **Ethyl acetate** was identified as a volatile component in fresh and used machine cutting-fluid emulsions at concentrations of 0.171 and 0.310 ug/g, respectively(3). **Ethyl acetate** was identified in the headspace of biodegradable and mixed household waste at concentrations ranging from 0.1 to 1 mg/cu m(4). It was also identified in liquid exudate from garden waste(5). **Ethyl acetate** has been identified as a volatile compound in the headspace of kitchen waste and mold-infested fiber board, kitchen waste exudate, stored food exudate, and garden waste headspace(6). **Ethyl acetate** was identified in 8 printer's inks at concentrations ranging from 0.1 to 13.7% (w/w)(7). **Ethyl acetate** was identified in volatile emissions from Scots pine(8). **Ethyl acetate** comprised 2.0 and 3.7% by weight of total organic gas emissions from industrial surface coatings and thinning solvent, respectively(9). Mean emission rates of **ethyl acetate** from particle board/carpet were 0.025 mg/sq m hr(10). **Ethyl acetate** emissions from whiskey vats averaged 0.593 g/cu m grain input(11). **Ethyl acetate** was found in glue used in Italian shoe factories(12). **Ethyl acetate** was identified as a volatile organic compound present in 3 of 3 samples of poultry manure at concentrations of 10.8, 23.0, and 61.2 mg/kg(13).

[(1) Isacoff H; Kirk-Othmer Encycl Chem Tech; 3rd ed. NY,NY: Wiley Interscience 7: 163 (1979) (2) Wallace LA et al; Res Triangle Inst, Research Triangle Park, NC Report 1991, USEPA/600/D-91/074; (NTIS PB-91-182865) (1991) (3) Yasuhara A et al; Agric Biol Chem 50: 1765-70 (1965) (4) Wilkins K; Chemosphere 29: 47-53 (1994) (5) Wilkins K, Larsen K; Chemosphere 32: 2049-55 (1996) (6) Wilkins CK, Larsen K; J High Resol Chromatogr 18: 373-7 (1995) (7) Rastogi SC; Arch Environ Contam Toxicol 20: 543-7 (1991) (8) Isidorov VA et al; Atmos Environ 19: 1-8 (1985) (9) Harley RA et al; Environ Sci Technol 26: 2395-408 (1992) (10) Colombo A et al; Sci Total Environ 91: 237-49 (1990) (11) Carter RV, Linsky B; Atmos Environ 8: 57-62 (1974) (12) Perbellini L et al; Med Lav 83: 115-19 (1992) (13) Yashuara A; J Chromatogr 387: 371-8 (1987)]**PEER REVIEWED**

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Environmental Fate/Exposure Summary:

Ethyl acetate's production and use as a pharmaceutic aid, in artificial fruit essences, and as a solvent may result in its release to the environment through various waste streams. If released to air, a vapor pressure of 93 mm Hg at 25 deg C indicates **ethyl acetate** will exist solely as a vapor in the ambient atmosphere. Vapor-phase **ethyl acetate** will be degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals; the half-life for this reaction in air is estimated to be 9.4 days. If released to soil, **ethyl acetate** is expected to have high mobility based upon an estimated Koc of 59. Volatilization from moist soil surfaces is expected to occur based upon a Henry's Law constant of 1.34X10-4 atm-cu m/mole. **Ethyl acetate's** vapor pressure indicates the potential for volatilization from dry soil surfaces exists. Biodegradation is expected to be an important process in both soil and water, based upon **ethyl acetate's** biodegradation in aqueous screening studies. 93% biodegradation was observed in a complete mix continuous-flow activated sludge system. 26.6 and 57.1% of **ethyl acetate'**s theoretical BOD was reached in 5 days using the standard dilution method and seawater dilution method, respectively. If released into water, **ethyl acetate** is not expected to adsorb to suspended solids and sediment in water based on the estimated Koc. Volatilization from water surfaces is expected to be an important fate process based on **ethyl acetate's** Henry's Law constant. Estimated volatilization half-lives for a model river and model lake are 8.9 hours and 5.6 days, respectively. An estimated BCF of 3.2 suggests the potential for bioconcentration in aquatic organisms is low. **Ethyl acetate's** hydrolysis half-life at 25 deg C and pH 7 is 2.0 years. Occupational exposure to **ethyl acetate** may occur through inhalation and dermal contact with this compound at workplaces where **ethyl acetate** is produced or used or where adhesives, thinners, degreasers, paints, inks, and dome reagents are used. The general population may be exposed to **ethyl acetate** via inhalation of ambient air, ingestion of food and drinking water, or dermal contact with consumer products containing this compound. (SRC)
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Natural Pollution Sources:

Ethyl acetate is a natural product of fermentation(1,2). Natural sources of **ethyl acetate** include animal waste, plant volatiles, and microbes(1).

[(1) Graedel TE; Chemical Compounds in the Atmosphere. NY,NY: Academic Press pp. 223-34 (1978) (2) Reed G; Kirk-Othmer Encycl Chem Tech; 3rd ed NY,NY: Wiley Interscience 24: 789 (1983)]**PEER REVIEWED**

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Artificial Pollution Sources:

Ethyl acetate's production and use as a pharmaceutic aid (flavor); in artificial fruit essences; as a solvent; in the manufacture of smokeless powder, artificial leather, and photographic films and plates; and in cleaning textiles(1) may result in its release to the environment through various waste streams(SRC).

[(1) Budavari S; The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. 12th ed. Whitehouse Station, NJ: Merck and Co Inc p 641 (1996)]**PEER REVIEWED**

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Environmental Fate:

TERRESTRIAL FATE: Based on a classification scheme(1), an estimated Koc value of 59(SRC), determined from a log Kow of 0.73(2) and a regression-derived equation(3), indicates that **ethyl acetate** is expected to have high mobility in soil(SRC). Volatilization of **ethyl acetate** from moist soil surfaces is expected to be important(SRC) given a Henry's Law constant of 1.34X10-4 atm-cu m/mole(4). The potential for volatilization of **ethyl acetate** from dry soil surfaces may exist(SRC) based on a vapor pressure of 93 mm Hg(5). **Ethyl acetate** may biodegrade in soil(SRC), based upon its biodegradation in aqueous screening studies(6,7).

[(1) Swann RL et al; Res Rev 85: 23 (1983) (2) Hansch C et al; Exploring QSAR. Hydrophobic, Electronic, and Steric Constants. ACS Professional Reference Book. Heller SR (consult ed) Washington,DC: Amer Chem Soc p. 9 (1995) (3) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington,DC: Amer Chem Soc pp. 4-9 (1990) (4) Butler JAV, Tamchandani CN; J Chem Soc: 952-5 (1935) (5) Daubert TE, Danner RP; Physical and Thermodynamic Properties of Pure Chemicals: Data Compilation. Design Inst Phys Prop Data, Amer Inst Chem Eng., NY,NY: Hemisphere Pub Corp, Vol 2 (1991) (6) Takemoto S et al; Suishitsu Odaka Kenkyu 4: 80-90 (1981) (7) Kincannon DF et al; J Water Pollut Control Fed 55: 157-63 (1983)]**PEER REVIEWED**

AQUATIC FATE: Based on a classification scheme(1), an estimated Koc value of 59(SRC), determined from a log Kow of 0.73(2) and a regression-derived equation(3), indicates that **ethyl acetate** is not expected to adsorb to suspended solids and sediment in water(SRC). **Ethyl acetate** is expected to volatilize from water surfaces(3,SRC) based on a Henry's Law constant of 1.34X10-4 atm-cu m/mole(4). Estimated volatilization half-lives for a model river and model lake are 8.9 hours and 5.6 days, respectively(3,SRC). According to a classification scheme(5), an estimated BCF of 3.2(3,SRC), from the log Kow(2), suggests the potential for bioconcentration in aquatic organisms is low(SRC). Simple esters are resistant to hydrolysis; **ethyl acetate's** hydrolysis half-life at 25 deg C and pH 7 is 2.0 years(6). Biodegradation is expected to be an important process in aquatic systems(SRC), based upon aqueous screening studies(7,8). **Ethyl acetate** reached 26.6 and 57.1% of its theoretical BOD in 5 days using the standard dilution method and seawater dilution method, respectively(7). 99.9% removal of **ethyl acetate** was observed in a complete mix continuous-flow activated sludge system; 93% of this removal was attributed to biodegradation(8). 94% of theoretical methane production was observed after incubation in sediment and groundwater collected from the methanogenic portion of an anoxic aquifer polluted by municipal landfill leachate(9).

[(1) Swann RL et al; Res Rev 85: 23 (1983) (2) Hansch C et al; Exploring QSAR. Hydrophobic, Electronic, and Steric Constants. ACS Professional Reference Book. Heller SR (consult ed) Washington,DC: Amer Chem Soc p 9 (1995) (3) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington,DC: Amer Chem Soc pp. 4-9, 5-4, 5-10, 15-1 to 15-29 (1990) (4) Butler JAV, Tamchandani CN; J Chem

Soc: 952-5 (1935) (5) Franke C et al; Chemosphere 29: 1501-14 (1994) (6) Mabey WR et al; J Phys Chem Ref Data Vol 7, No. 2 p. 411 (1978) (7) Takemoto S et al; Suishitsu Odaka Kenkyu 4: 80-90 (1981) (8) Kincannon DF et al; J Water Pollut Control Fed 55: 157-63 (1983) (9) Sulfita JM, Mormile MR; Environ Sci Technol 27: 976-8 (1993)]**PEER REVIEWED**

ATMOSPHERIC FATE: According to a model of gas/particle partitioning of semivolatile organic compounds in the atmosphere(1), **ethyl acetate,** which has a vapor pressure of 93 mm Hg at 25 deg C(2), is expected to exist solely as a vapor in the ambient atmosphere. Vapor-phase **ethyl acetate** is degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals(SRC); the half-life for this reaction in air is estimated to be 10 days(3,SRC).
[(1) Bidleman TF; Environ Sci Technol 22: 361-367 (1988) (2) Daubert TE, Danner RP; Physical and Thermodynamic Properties of Pure Chemicals: Data Compilation. Design Inst Phys Prop Data, Amer Inst Chem Eng., NY,NY: Hemisphere Pub Corp, Vol 2 (1991) (3) Atkinson R; J Phys Chem Ref Data Monograph 1 p. 166 (1989)]**PEER REVIEWED**

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Environmental Biodegradation:

ANAEROBIC: **Ethyl acetate** has been demonstrated to be amenable to anaerobic biodegradation(1). It was mineralized (>75% of theoretical methane production) in 10% sludge from a secondary digester within 8 weeks(2). 96% utilization occurred in an anaerobic reactor with a 20 day retention time(3). **Ethyl acetate,** at a concentration of 1000 mg/l, was readily degraded in batch reactors containing anaerobic solids from an industrial anaerobic digester with some exposure to **ethyl acetate(**4). 100% loss of **ethyl acetate** was observed in aquifer slurries amended with sulfate and nitrate following 244 days and 85 days incubation, respectively(5). 94% of theoretical methane production was observed after incubation in sediment and groundwater collected from the methanogenic portion of an anoxic aquifer polluted by municipal landfill leachate(6).

[(1) Speece RE; Environ Sci Tech 17: 416A-27A (1983) (2) Shelton DR, Tiedje JM; Appl Environ Microbiol 47: 850-7 (1984) (3) Chou WL et al; Biotech Bioeng Symp 8: 391-414 (1979) (4) Schwartz LJ; Appl Biochem Biotehcnol 28/29: 297-305 (1991) (5) Mormile MR et al; Environ Sci Technol 28: 1727-32 (1994) (6) Sulfita JM, Mormile MR; Environ Sci Technol 27: 976-8 (1993)]**PEER REVIEWED**

A review concluded that **ethyl acetate** is easily removed by biological treatment(1). Reported 5 day BOD values using a sewage inoculum range from 36-68% of theoretical(2-5) with the value being somewhat reduced in salt water(2). One investigator reported that **ethyl acetate** was completely degraded in 20 hr using activated sludge(6). In a bench-scale continuous-flow activated sludge reactor with an 8 hour retention time, 99.9% removal (including 17% volatilization loss) was obtained, with 80% of the theoretical BOD(7). **Ethyl acetate** was 90% biooxidized in a 20-day BOD test using a filtered raw sewage seed; it was biooxidized 77% in a 28-day OECD closed-bottle test(8). A screening procedure that was systematically applied to a large number of organic chemicals ranked **ethyl acetate** as being completely biodegraded in a short time by general microorganisms(9). After a 5 hr lag, 43 to 53% of theoretical BOD was obtained in 50 to 70 hr(9). In screening tests, **ethyl acetate,** present at a concentration of 5 ppm, reached 26.6 and 57.1% of its theoretical BOD in 5 days using the standard dilution method and seawater dilution method, respectively(10). 99.9% removal of **ethyl acetate** was observed in a complete mix continuous-flow activated sludge system; 93% of this removal was attributed to biodegradation(11).

[(1) Thom NS, Agg AR; Proc Roy Soc London B 189: 347-57 (1975) (2) Price KS et al; J Water Pollut Control Fed 46: 63-77 (1974) (3) Ettinger MB; Ind Eng Chem 48: 256-9 (1956) (4) Young RHF et al; J Water Pollut Control Fed 40: 354-68 (1968) (5) Heukelekian H, Rand MC; J Water Pollut Control Assoc 29: 1040-53 (1955) (6) Slave T et al; Rev Chim 25: 666-70 (1974) (7) Stover EL, Kincannon DF; J Water Pollut Control Fed 55: 97-109 (1983) (8) Waggy GT et al; Environ Toxicol Chem 13: 1277-80 (1994) (9) Urano K, Kato Z; J Haz Mat 13: 135-45, 147-59 (1986) (10) Takemoto S et al; Suishitsu Odaka Kenkyu 4: 80-90 (1981) (11) Kincannon DF et al; J Water Pollut Control Fed 55: 157-63

(1983)]**PEER REVIEWED**

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Environmental Abiotic Degradation:

The rate constant for the vapor-phase reaction of **ethyl acetate** with photochemically-produced hydroxyl radicals is 1.6X10-12 cu cm/molecule-sec at 25 deg C(1). This corresponds to an atmospheric half-life of about 10 days at an atmospheric concentration of 5X10+5 hydroxyl radicals per cu cm(1,SRC). The observed rate constant for the vapor-phase reaction of **ethyl acetate** with nitrate radicals is 1.4X10-17 cu cm/molecule-sec(2). This corresponds to an atmospheric half-life of about 16 years at an average nighttime nitrate radical concentration of 2X10+8 molecules/cu cm (nitrate radicals are unstable in sunlight)(3,SRC). The rate constant for the reaction of **ethyl acetate** with hydroxyl radicals in aqueous solution is 4.0X10+8 L/mol sec(4). This corresponds to a half-life of about 5.5 years(SRC) at an average aqueous hydroxyl radical concentration of 1X10-17 mol/l(5). Simple esters are resistant to hydrolysis; **ethyl acetate's** hydrolysis half-life at 25 deg C and pH 7 is 2.0 years(6).
[(1) Atkinson R; J Phys Chem Ref Data Monograph 1 p. 166 (1989) (2) Atkinson R; J Phys Chem Ref Data Monograph p. 213 (1994) (3) GEMS; Graphical Exposure Modeling System. FAP. Fate of Atmos Pollut (1986) (4) Buxton GV et al; J Phys Chem Ref Data 17: 513-882 (1988) (5) Mill T et al; Science 207: 886-7 (1980) (6) Mabey WR et al; J Phys Chem Ref Data Vol 7, No. 2 p. 411 (1978)]**PEER REVIEWED**

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Environmental Bioconcentration:

An estimated BCF of 3.2 was calculated for **ethyl acetate(**SRC), using a log Kow of 0.73(1) and a regression-derived equation(2). According to a classification scheme(3), this BCF suggests the potential for bioconcentration in aquatic organisms is low(SRC).

[(1) Hansch C et al; Exploring QSAR. Hydrophobic, Electronic, and Steric Constants. ACS Prof Ref Book. Heller SR (consult ed) Washington,DC: Amer Chem Soc p. 9 (1995) (2) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington DC: Amer Chem Soc pp. 5-4, 5-10 (1990) (3) Franke C et al; Chemosphere 29: 1501-14 (1994)]**PEER REVIEWED**

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Soil Adsorption/Mobility:

The Koc of **ethyl acetate** is estimated as 59(SRC), using a log Kow of 0.73(1) and a regression-derived equation(2,SRC). According to a classification scheme(3), this estimated Koc value suggests that **ethyl acetate** is expected to have high mobility in soil(SRC).

[(1) Hansch C et al; Exploring QSAR. Hydrophobic, Electronic, and Steric Constants. ACS Prof Ref Book. Heller SR (consult ed) Washington,DC: Amer Chem Soc p. 9 (1995) (2) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington,DC: Amer Chem Soc pp. 4-9 (1990) (3) Swann RL et al; Res Rev 85: 23 (1983)]**PEER REVIEWED**

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Volatilization from Water/Soil:

The Henry's Law constant for **ethyl acetate** is 1.34X10-4 atm-cu m/mole(1). This Henry's Law constant indicates that **ethyl acetate** is expected to volatilize from water surfaces(2,SRC). Based on this Henry's Law constant, the estimated volatilization half-life from a model river (1 m deep, flowing 1 m/sec, wind velocity of 3 m/sec) is estimated as 8.9 hours(2,SRC). The estimated volatilization half-life from a model lake (1 m deep, flowing 0.05 m/sec, wind velocity of 0.5 m/sec) is estimated as 5.6 days(2,SRC). **Ethyl acetate's** Henry's Law constant(1) indicates that volatilization from moist soil surfaces may occur(SRC). The potential for volatilization of **ethyl acetate** from dry soil surfaces may exist(SRC) based on a vapor pressure of 93 mm Hg(3). 7% of the 99.9% removal observed in a continuous flow activated sludge system was attributed to stripping(4).

[(1) Butler JAV, Tamchandani CN; J Chem Soc: 952-5 (1935) (2) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington,DC: Amer Chem Soc pp. 15-1 to 15-29 (1990) (3) Daubert TE, Danner RP; Physical and Thermodynamic Properties of Pure Chemicals: Data Compilation. Design Inst Phys Prop Data, Amer Inst Chem Eng., NY,NY: Hemisphere Pub Corp, Vol 2 (1991) (4) Kincannon DF et al; J Water Pollut Control Fed 55: 157-63 (1983)]**PEER REVIEWED**

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Environmental Water Concentrations:

DRINKING WATER: **Ethyl acetate** was detected, not quantified in 3 New Orleans drinking water plants(1). It was detected in drinking water, no levels given(2). **Ethyl acetate** was identified in commercially bottled Artesian water(3).

[(1) Keith LH et al; pp. 329-73 in Identification and Analysis of Organic Pollutants in Water Keith LH ed Ann Arbor Press, Ann Arbor MI (1976) (2) Kool HJ et al; Crit Rev Environ Control 12: 307-57 (1982) (3) Dowty BJ et al; Environ Sci Technol 9: 762-5 (1975)]**PEER REVIEWED**

GROUNDWATER: It was not detected in an aquifer polluted by a paint factory even though **ethyl acetate** was stored in buried tanks that leaked(1).

[(1) Botta D et al; Comm Eur Com Eur 8518 (Anal Org Micropollut Water): 261-75 (1984)]**PEER REVIEWED**

SURFACE WATER: 14 heavily industrialized river basins in USA (204 sites)-only 1 site (Delaware River Basin) positive-1 ppb(1). Hayashida River in Tatsumo City, Japan (site of leather industry) 585 ppb(2). **Ethyl acetate** was identified in water samples from the brook, Rickenbach East, Switzerland, which receives discharges from a paint factory(3).

[(1) Ewing BB et al; Monitoring to Detect Previously Unrecognized Pollutants in Surface Waters p. 75 USEPA-560/6-77-015 (1977) (2) Yasuhara A et al; Environ Sci Technol 15: 570-3 (1981) (3) Juettner F; Wat Sci Tech 25: 155-64 (1992)]**PEER REVIEWED**

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Effluent Concentrations:

Effluent gas from the metal painting factory and from the lumber painting factory contained **ethyl acetate.**
[Yasuhara A et al; Chemosphere 13 (3): 469-82 (1984)]**PEER REVIEWED**

Ethyl acetate was detected, not quantified in oil refinery final effluent(1) and effluent from sewage treatment plants(2). **Ethyl acetate** has been detected in U.S. municipal landfill leachate at concentrations ranging from 42 to 290 g/l(3). **Ethyl acetate** was identified, but not quantified, in hazardous waste samples from a Midwest remedial action site(4). **Ethyl acetate** was detected, but not quantified, in a grab sample of oil refinery final effluent from a refinery in Lockport, IL(5). **Ethyl acetate** was identified as a volatile organic compound in a composite waste sample obtained from a barge which dumped its waste on Feb 9, 1978 at the Puerto Rico dumpsite(6). **Ethyl acetate** was identified in flue gas from a waste incineration plant in Germany(7).
[(1) Ellis DD et al; Arch Environ Contam Toxicol 11: 373-82 (1982) (2) Shackelford WM, Keith LH; Frequency of Organic Compounds Identified in Water USEPA-600/4-76-062 (1976) (3) Roy WR; Contam Groundwaters, Adriano DC et al eds, Sci Rev: Northwood, UK 411-46 (1994) (4) Puskar MA et al; Environ Sci Technol 21: 90-6 (1987) (5) Ellis DD et al; Arch Environ Contam Toxicol 11: 373-82 (1982) (6) Brooks JM et al; Wastes Ocean, Vol 1, Duedall, IW ed, NY,NY: Wiley pp. 171-98 (1983) (7) Jay K, Stieglitz L; Chemosphere 30: 1249-60 (1995)]**PEER REVIEWED**

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Atmospheric Concentrations:

URBAN/SUBURBAN: **Ethyl acetate** was detected, not quantified in Leningrad, USSR(1). Average concentrations of **ethyl acetate** in urban air samples collected from four different sites in Stockholm ranged from 0.27 to 2.64 ppb; the average concentration at a site 12 km outside Stockholm was 0.23 ppb(2). It was identified in ambient air from Pasadena, TX, Houston, TX, and Glendora, CA(3). SOURCE AREAS: It was detected in ambient air surrounding Kin Buc waste disposal site (4 sites) 0, trace, 4.1, 230 ug/cu m(4). **Ethyl acetate** was detected in ambient air near a furnace used for incinerating paint wastes at a concentration of 0.7 ppbv(5).
[(1) Ioffe BV et al; J Chromatogr 142: 787-95 (1977) (2) Jonsson AE et al; Environ Int 11: 383-92 (1985) (3) Pellizarri ED; Development of Analytical Techniques for Measuring Ambient Atmospheric Carcinogenic Vapors, EPA-600/2-75-076 (1975) (4) Pellizarri ED; Environ Sci Technol 16: 781-5 (1982) (5) Kelly TJ et al; Environ Sci Technol 27: 1146-53 (1993)]**PEER REVIEWED**

OTHER: 5 out of 8 personal air samples collected from volunteers in Bayonne and Elizabeth, NJ between July and Dec 1980 contained **ethyl acetate** at unreported concentrations(1). **Ethyl acetate** was identified in air at a forest site in the Eggegebirge in North Rhine-Westfalia, West Germany(2). INDOOR: **Ethyl acetate** was detected in air samples taken from preschools in Stockholm(3). **Ethyl acetate** was detected in indoor air samples from Northern Italy at concentrations of 9 and 26 ug/cu m(4). It was detected in indoor air collected in a machine shop and a new office area at concentrations of 1.4 and 21.8 ppbv, respectively(5). **Ethyl acetate** was detected in the indoor air of 12 out of 12 Canadian homes in Nov and Dec 1986 at concentrations ranging from 3 to 13 ug/cu m, average 8.9 ug/cu m; indoor air concentrations in 6 Canadian homes in Feb and March 1987 ranged from 7 to 494 ug/cu m, average 153 ug/cu m (outdoor air average concentration 10 ug/cu m)(6). **Ethyl acetate** was detected in indoor air of new and recently renovated buildings in Switzerland at a maximum concentration of 1052 ug/cu m(7). It was detected in at least one indoor air sample from 17 locations from two Stockholm preschools(8).
[(1) Wallace LA et al; Environ Res 35: 293-319 (1984) (2) Helmig D et al; Chemosphere 19: 1399-1412 (1989) (3) Noma E et al; Atmos Environ 22: 451-60 (1988) (4) DeBortoli M et al; Environ Int 12: 343-50 (1986) (5) Kelly TJ et al; Environ Sci Technol 27: 1146-53 (1993) (6) Chan CC et al; J Air Waste Manage Assoc 40: 62-7 (1990) (7) Rothweiler H et al; Atmos Environ 26A: 2219-25 (1992) (8) Noma E et al; Aimos Environ 22: 451-60 (1988)]**PEER REVIEWED**

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Food Survey Values:

Ethyl acetate forms from the reaction of acetyl coenzyme A with ethanol, and its formation depends greatly on temperature. Maximum formation occurs at 20-25 deg C. Therefore, top fermented beers contain higher amounts of this ester.
[Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984.,p. V24 789 (1984)]**PEER REVIEWED**

Ethyl acetate is found in USA lager beer, 25 to 50 ppm(1). It is a component of Orleans vinegar(2) and artificial grape flavoring(3). **Ethyl acetate** was identified as a volatile component of roasted filberts(4), fried bacon(5), Beaufort cheese(6), blue cheese(7), Idaho Russet Burbank baked potatoes(8), and the edible Korean chamchwi plant(9). Korean salt-fermented anchovy, big-eyed herring, hair tail viscera and shrimp pastes contained **ethyl acetate** at mean concentrations of 3490, 1660, 2340, and 3750 ng/g, respectively(10). **Ethyl acetate** was detected in beer at a concentration of 8 ppm(11). **Ethyl acetate** was identified as a volatile compound in kiwi fruit, comprising 3.9, 4.7, and 1.6% of the components in mature, ripe, and very ripe fruit, respectively(12). It was also identified as a volatile component of pineapple guava at a concentration of 0.11 ug/g(13). Fresh grapefruit juice contained 1.65 ppm **ethyl acetate(**14). **Ethyl acetate** was identified in mature and overripe guava fruits at concentrations of 614.1 and 8884.2 ug/kg, respectively(15). It was identified as a volatile flavor component of the strawberry variety Sivetta and in Golden Delicious apples(16).
[(1) Reed G; Kirk-Othmer Encycl Chem Tech 3rd ed. NY,NY: Wiley Interscience 24: 789 (1983) (2) Webb AD; Kirk-Othmer Encycl Chem Tech 3rd ed. NY,NY: Wiley Interscience 23: 757 (1983) (3) Jones MB; Kirk-Othmer Encycl Chem Tech 3rd ed. NY,NY: Wiley Interscience 4: 712 (1978) (4) Kinlin TE et al; J Agric Food Chem 20: 1021-8 (1972) (5) Ho CT et al; J Agric Food Chem 31: 336-42 (1983) (6) Dumont JP, Adda J; J Agric Food Chem 26: 364-7 (1978) (7) Day EA, Anderson DF; J Agric Food Chem 13: 2-4 (1965) (8) Coleman EC et al; J Agric Food Chem 29: 42-8 (1981) (9) Chung TY et al; J Agric Food Chem 41: 1693-7 (1993) (10) Cha YJ, Cadwallader KR; J Food Sci 60: 19-24 (1995) (11) Hashimoto H, Kuroiwa YJ; J Inst Brewing 72: 151-62 (1966) (12) Bartley JP, Schwede AM; J Agric Food Chem 37: 1023-5 (1989) (13) Binder RG, Flath RA; J Agric Food Chem 37: 734-6 (1989) (14) Cadwallader KR, Xu Y; J Agric Food Chem 42: 782-4 (1994) (15) Chyau CC et al; J Agric Food Chem 40: 846-9 (1992) (16) Dirinck P et al; Analysis of Volatiles, Berlin,Germany: Walter Degruyter and Co 381-400 (1984)]**PEER REVIEWED**

Ethyl acetate was identified as a volatile component of duck meat, duck fat, Cantonese style roasted duck, and Cantonese style roasted duck gravy at concentrations of <0.05, 2.43, 23.94, and <0.05 ppb wet weight, respectively(1). It was identified as a volatile compound in fried chicken flavor(2), nectarines(3), Concord grape essence(4), three Conn Creek wines(5), Sukiyaki(6), bananas(7), and floured Chickpea

seed(8). **Ethyl acetate** was detected in fresh hand-squeezed (mechanically) unpasteurized orange juice from five different cultivars and one hybrid at concentrations of, ppm: 0.28 (0.15 to 0.25) in Valencia oranges; 0.17 to 0.23 (0.15) in Pineapple oranges; 0.12 to 0.13 in Hamlin oranges; 0.77 in Florida navel oranges; 0.17 in California navel oranges; 0.28 in Pera oranges; and 0.12 (0.082) in Ambersweet oranges(9). Large amounts of **ethyl acetate** were detected in headspace from Bisbee Delicious apples at the earliest harvests(10).
[(1) Wu CM, Liou SE; J Agric Food Chem 40: 838-41 (1992) (2) Tang J et al; J Agric Food Chem 31: 1287-92 (1983) (3) Takeoka GR et al; J Agric Food Chem 36: 553-60 (1988) (4) Stevens KL et al; J Food Sci 30: 1006-7 (1965) (5) Shimoda M et al; J Agric Food Chem 41: 1664-66 (1993) (6) Shibamoto T et al; J Agric Food Chem 29: 57-63 (1981) (7) Macku C, Jennings WG; J Agric Food Chem 35: 845-8 (1987) (8) Rembold H et al; J Agric Food Chem 37: 659-62 (1989) (9) Moshonas MG, Shaw PE; J Agric Food Chem 42: 1525-8 (1994) (10) Mattheis JP et al; J Agric Food Chem 39: 1902-6 (1991)]**PEER REVIEWED**

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Plant Concentrations:

Ethyl acetate was identified as a volatile component of kiwi fruit flowers(1). Volatile emissions from Scots pine were found to contain **ethyl acetate(**2).

[(1) Tatsuka K et al; J Agric Food Chem 38: 2176-80 (1990) (2) Singh HB, Zimmerman PB; Adv Environ Sci Technol 24: 177-235 (1992)]**PEER REVIEWED**

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Fish/Seafood Concentrations:

Ethyl acetate was identified in a sample of mussel collected from the Oarai Coast in Ibaraki, Japan on July 31, 1985 at a concentration of 97.1 ug/g(1).

[(1) Yashuara A, Morita M; Chemosphere 16: 2559-65 (1987)]**PEER REVIEWED**

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Milk Concentrations:

Mother's milk from 4 urban areas in the USA, 1 of 8 samples positive(1).

[(1) Pellizarri ED et al; Environ Sci Technol 16: 781-5 (1982)]**PEER REVIEWED**

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Other Environmental Concentrations:

Nail polish remover typically contains 40 wt% **ethyl acetate(**1,2). **Ethyl acetate** was identified as a volatile component in fresh and used machine cutting-fluid emulsions at concentrations of 0.171 and 0.310 ug/g, respectively(3). **Ethyl acetate** was identified in the headspace of biodegradable and mixed household waste at concentrations ranging from 0.1 to 1 mg/cu m(4). It was also identified in liquid exudate from garden waste(5). **Ethyl acetate** has been identified as a volatile compound in the headspace of kitchen waste and mold-infested fiber board, kitchen waste exudate, stored food exudate, and garden waste headspace(6). **Ethyl acetate** was identified in 8 printer's inks at concentrations ranging from 0.1 to 13.7% (w/w)(7). **Ethyl acetate** was identified in volatile emissions from Scots pine(8). **Ethyl acetate** comprised 2.0 and 3.7% by weight of total organic gas emissions from industrial surface coatings and thinning solvent, respectively(9). Mean emission rates of **ethyl acetate** from particle board/carpet were 0.025 mg/sq m hr(10). **Ethyl acetate** emissions from whiskey vats averaged 0.593 g/cu m grain input(11). **Ethyl acetate** was found in glue used in Italian shoe factories(12). **Ethyl acetate** was identified as a volatile organic compound present in 3 of 3 samples of poultry manure at concentrations of 10.8, 23.0, and 61.2 mg/kg(13).

[(1) Isacoff H; Kirk-Othmer Encycl Chem Tech; 3rd ed. NY,NY: Wiley Interscience 7: 163 (1979) (2) Wallace LA et al; Res Triangle Inst, Research Triangle Park, NC Report 1991, USEPA/600/D-91/074; (NTIS PB-91-182865) (1991) (3) Yasuhara A et al; Agric Biol Chem 50: 1765-70 (1965) (4) Wilkins K; Chemosphere 29: 47-53 (1994) (5) Wilkins K, Larsen K; Chemosphere 32: 2049-55 (1996) (6) Wilkins CK, Larsen K; J High Resol Chromatogr 18: 373-7 (1995) (7) Rastogi SC; Arch Environ Contam Toxicol 20: 543-7 (1991) (8) Isidorov VA et al; Atmos Environ 19: 1-8 (1985) (9) Harley RA et al; Environ Sci Technol 26: 2395-408 (1992) (10) Colombo A et al; Sci Total Environ 91: 237-49 (1990) (11) Carter RV, Linsky B; Atmos Environ 8: 57-62 (1974) (12) Perbellini L et al; Med Lav 83: 115-19 (1992) (13) Yashuara A; J Chromatogr 387: 371-8 (1987)]**PEER REVIEWED**

ETHYL ACETATE

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For other data, click on the Table of Contents

Environmental Standards & Regulations:

FIFRA Requirements:

Residues of **ethyl acetate** are exempted from the requirement of a tolerance when used as a solvent or cosolvent in accordance with good agricultural practices as inert (or occasionally active) ingredients in pesticide formulations applied to growing crops or to raw agricultural commodities after harvest.
[40 CFR 180.1001(c) (7/1/97)]**PEER REVIEWED**

As the federal pesticide law FIFRA directs, EPA is conducting a comprehensive review of older pesticides to consider their health and environmental effects and make decisions about their future use. Under this pesticide reregistration program, EPA examines health and safety data for pesticide active ingredients initially registered before November 1, 1984, and determines whether they are eligible for reregistration. In addition, all pesticides must meet the new safety standard of the Food Quality Protection Act of 1996. Pesticides for which EPA had not issued Registration Standards prior to the effective date of FIFRA, as amended in 1988, were divided into three lists based upon their potential for human exposure and other factors, with List B containing pesticides of greater concern and List D pesticides of less concern. **Ethyl acetate** is found on List D. Case No: 4005; Pesticide type: insecticide, herbicide, antimicrobial; Case Status: OPP is reviewing data from the pesticide's producers regarding its human health and/or environmental effects, or OPP is determining the pesticide's eligibility for reregistration and developing the Reregistration Eligibility Decision (RED) document.; Active ingredient (AI): **Ethyl acetate;** AI Status: The active ingredient is no longer contained in any registered pesticide products ... "cancelled."
[USEPA/OPP; Status of Pesticides in Registration, Reregistration and Special Review p.292 (Spring, 1998) EPA 738-R-98-002]**QC REVIEWED**

TSCA Requirements:

A testing consent order is in effect for **ethyl acetate** for health effects testing. FR citation: 1/23/95.
[40 CFR 799.5000 (7/1/97)]**PEER REVIEWED**

CERCLA Reportable Quantities:

Persons in charge of vessels or facilities are required to notify the National Response Center (NRC) immediately, when there is a release of this designated hazardous substance, in an amount equal to or greater than its reportable quantity of 5000 lb or 2270 kg. The toll free number of the NRC is (800) 424-8802; In the Washington D.C. metropolitan area (202) 426-2675. The rule for determining when notification is required is stated in 40 CFR 302.4 (section IV. D.3.b).
[40 CFR 302.4 (7/1/97)]**PEER REVIEWED**

RCRA Requirements:

U112; As stipulated in 40 CFR 261.33, when **ethyl acetate,** as a commercial chemical product or manufacturing chemical intermediate or an off-specification commercial chemical product or a manufacturing chemical intermediate, becomes a waste, it must be managed according to Federal and/or

State hazardous waste regulations. Also defined as a hazardous waste is any residue, contaminated soil, water, or other debris resulting from the cleanup of a spill, into water or on dry land, of this waste. Generators of small quantities of this waste may qualify for partial exclusion from hazardous waste regulations (40 CFR 261.5).
[40 CFR 261.33 (7/1/97)]**PEER REVIEWED**

F003; When **ethyl acetate** is a spent solvent, it is classified as a hazardous waste from a nonspecific source (F003), as stated in 40 CFR 261.31, and must be managed according to State and/or Federal hazardous waste regulations.
[40 CFR 261.31 (7/1/97)]**PEER REVIEWED**

Atmospheric Standards:

This action promulgates standards of performance for equipment leaks of Volatile Organic Compounds (VOC) in the Synthetic Organic Chemical Manufacturing Industry (SOCMI). The intended effect of these standards is to require all newly constructed, modified, and reconstructed SOCMI process units to use the best demonstrated system of continuous emission reduction for equipment leaks of VOC, considering costs, non air quality health and environmental impact and energy requirements. **Ethyl acetate** is produced, as an intermediate or final product, by process units covered under this subpart.
[40 CFR 60.489 (7/1/97)]**PEER REVIEWED**

FDA Requirements:

Certification of this color additive when used as a diluent (in inks for marking fruit & vegetables) is not necessary for the protection of the public health and therefore batches thereof are exempt from the requirements of section 706(c) of the Federal Food, Drug, and Cosmetic Act. /Restrictions incl no residue./
[21 CFR 73.1 (4/1/97)]**PEER REVIEWED**

Synthetic flavoring substances and adjuvants /for human consumption/ that are generally recognized as safe for their intended use, within the meaning of section 409 of the Act. **Ethyl acetate** is included on this list.
[21 CFR 182.60 (4/1/97)]**PEER REVIEWED**

Synthetic flavoring substances and adjuvants /for animal drugs, feeds, and related products/ that are generally recognized as safe for their intended use, within the meaning of section 409 of the Act. **Ethyl acetate** is included on this list.
[21 CFR 582.60 (4/1/97)]**PEER REVIEWED**

Allowable Tolerances:

Residues of **ethyl acetate** are exempted from the requirement of a tolerance when used as a solvent or cosolvent in accordance with good agricultural practices as inert (or occasionally active) ingredients in pesticide formulations applied to growing crops or to raw agricultural commodities after harvest.
[40 CFR 180.1001(c) (7/1/97)]**PEER REVIEWED**

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[USEPA/OPP; Status of Pesticides in Registration, Reregistration and Special Review p.292 (Spring, 1998) EPA 738-R-98-002]**QC REVIEWED**

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ETHYL ACETATE

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[40 CFR 302.4 (7/1/97)]**PEER REVIEWED**

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[40 CFR 261.33 (7/1/97)]**PEER REVIEWED**

F003; When **ethyl acetate** is a spent solvent, it is classified as a hazardous waste from a nonspecific source (F003), as stated in 40 CFR 261.31, and must be managed according to State and/or Federal hazardous waste regulations.
[40 CFR 261.31 (7/1/97)]**PEER REVIEWED**

ETHYL ACETATE

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ETHYL ACETATE

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[21 CFR 73.1 (4/1/97)]**PEER REVIEWED**

Synthetic flavoring substances and adjuvants /for human consumption/ that are generally recognized as safe for their intended use, within the meaning of section 409 of the Act. **Ethyl acetate** is included on this list.
[21 CFR 182.60 (4/1/97)]**PEER REVIEWED**

Synthetic flavoring substances and adjuvants /for animal drugs, feeds, and related products/ that are generally recognized as safe for their intended use, within the meaning of section 409 of the Act. **Ethyl acetate** is included on this list.
[21 CFR 582.60 (4/1/97)]**PEER REVIEWED**

ETHYL ACETATE

CASRN: 141-78-6

For other data, click on the Table of Contents

Allowable Tolerances:

Residues of **ethyl acetate** are exempted from the requirement of a tolerance when used as a solvent or cosolvent in accordance with good agricultural practices as inert (or occasionally active) ingredients in pesticide formulations applied to growing crops or to raw agricultural commodities after harvest.
[40 CFR 180.1001(c) (7/1/97)]**PEER REVIEWED**

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Chemical/Physical Properties:

Molecular Formula:

C4-H8-O2

[The Merck Index. 10th ed. Rahway, New Jersey: Merck Co., Inc., 1983. 545]**PEER REVIEWED**

Molecular Weight:

88.11

[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 641]**PEER REVIEWED**

Color/Form:

CLEAR LIQUID

[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 641]**PEER REVIEWED**

Colorless liquid.

[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 94-116. Washington, D.C.: U.S. Government Printing Office, June 1994. 130]**PEER REVIEWED**

Odor:

CHARACTERISTIC ETHER-LIKE ODOR REMINISCENT OF PINEAPPLE.

[Fenaroli's Handbook of Flavor Ingredients. Volume 2. Edited, translated, and revised by T.E. Furia and N. Bellanca. 2nd ed. Cleveland: The Chemical Rubber Co., 1975. 157]**PEER REVIEWED**

Fragrant odor

[Sax, N.I. Dangerous Properties of Industrial Materials. 6th ed. New York, NY: Van Nostrand Reinhold, 1984. 1315]**PEER REVIEWED**

Ether-like, fruity odor.

[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 94-116. Washington, D.C.: U.S. Government Printing Office, June 1994. 130]**PEER REVIEWED**

Fruity with a brandy note.

[Gerhartz, W. (exec ed.). Ullmann's Encyclopedia of Industrial Chemistry. 5th ed.Vol A1: Deerfield Beach, FL: VCH Publishers, 1985 to

Present.,p. VA11 152]**PEER REVIEWED**

Taste:

PLEASANT TASTE WHEN DILUTED.
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 641]**PEER REVIEWED**

BITTERSWEET, WINE-LIKE BURNING TASTE.
[Fenaroli's Handbook of Flavor Ingredients. Volume 2. Edited, translated, and revised by T.E. Furia and N. Bellanca. 2nd ed. Cleveland: The Chemical Rubber Co., 1975. 157]**PEER REVIEWED**

Ethyl acetate ... contributes a fruity flavor to beer.
[Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984.,p. 24 789 (1984)]**PEER REVIEWED**

Boiling Point:

77 DEG C
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 641]**PEER REVIEWED**

Melting Point:

-83 DEG C
[Weast, R.C. (ed.) Handbook of Chemistry and Physics. 69th ed. Boca Raton, FL: CRC Press Inc., 1988-1989.,p. C-48]**PEER REVIEWED**

Critical Temperature & Pressure:

Critical temperature: 250 DEG C; Critical pressure: 3.8 MN/SQ M
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Density/Specific Gravity:

Sp gr: 0.902 AT 20 DEG C/4 DEG C
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 641]**PEER REVIEWED**

Heat of Combustion:

-5616 CAL/G
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing

Office, 1984-5.]**PEER REVIEWED**

Heat of Vaporization:

87.6 CAL/G
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Octanol/Water Partition Coefficient:

log Kow= 0.73
[Hansch, C., Leo, A., D. Hoekman. Exploring QSAR - Hydrophobic, Electronic, and Steric Constants. Washington, DC: American Chemical Society., 1995. 9]**PEER REVIEWED**

Solubilities:

SOL IN ALCOHOL, ETHER, ACETONE, AND BENZENE
[Weast, R.C. (ed.) Handbook of Chemistry and Physics. 69th ed. Boca Raton, FL: CRC Press Inc., 1988-1989.,p. C-48]**PEER REVIEWED**

MISCIBLE WITH CHLOROFORM
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 641]**PEER REVIEWED**

MISCIBLE IN FIXED & VOLATILE OILS.
[Osol, A. (ed.). Remington's Pharmaceutical Sciences. 16th ed. Easton, Pennsylvania: Mack Publishing Co., 1980. 1232]**PEER REVIEWED**

Very soluble in water (64 g/l at 25 deg C)
[Wasik SP et al; Octanol/Water Partition Coefficients and Aqueous Solubilities of Organic Compounds p.66 NBS TR81-2406 (1981)]**PEER REVIEWED**

Miscible with oxygenated and chlorinated solvents.
[Ashford, R.D. Ashford's Dictionary of Industrial Chemicals. London, England: Wavelength Publications Ltd., 1994. 387]**PEER REVIEWED**

In water, 8.01X10+4 mg/l at 25 deg C.
[Yalkowsky SH, Dannenfelser RM; Aquasol Database of Aqueous Solubility. Version 5. College of Pharmacy, Univ of Ariz - Tucson, AZ. PC Version (1992)]**PEER REVIEWED**

Spectral Properties:

Index of Refraction = 1.3719 at 20 deg C/D
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc.,

1996. 641]**PEER REVIEWED**

MAX ABSORPTION (METHANOL): 209 NM (LOG E= 1.86); SADTLER REFERENCE NUMBER: 4 (IR, PRISM); 3 (IR, GRATING)
[Weast, R.C. (ed.). Handbook of Chemistry and Physics. 60th ed. Boca Raton, Florida: CRC Press Inc., 1979.,p. C-86]**PEER REVIEWED**

IR: 4802 (Coblentz Society Spectral Collection)
[Weast, R.C. and M.J. Astle. CRC Handbook of Data on Organic Compounds. Volumes I and II. Boca Raton, FL: CRC Press Inc. 1985.,p. V1 18]**PEER REVIEWED**

UV: 4-21 (Organic Electronic Spectral Data, Phillips et al, John Wiley & Sons, New York)
[Weast, R.C. and M.J. Astle. CRC Handbook of Data on Organic Compounds. Volumes I and II. Boca Raton, FL: CRC Press Inc. 1985.,p. V1 18]**PEER REVIEWED**

NMR: 79 (Varian Associates NMR Spectra Catalogue)
[Weast, R.C. and M.J. Astle. CRC Handbook of Data on Organic Compounds. Volumes I and II. Boca Raton, FL: CRC Press Inc. 1985.,p. V1 18]**PEER REVIEWED**

MASS: 158 (Atlas of Mass Spectral Data, John Wiley & Sons, New York)
[Weast, R.C. and M.J. Astle. CRC Handbook of Data on Organic Compounds. Volumes I and II. Boca Raton, FL: CRC Press Inc. 1985.,p. V1 18]**PEER REVIEWED**

Intense mass spectral peaks: 43 m/z, 61 m/z, 70 m/z, 73 m/z, 88 m/z
[Pfleger, K., H. Maurer and A. Weber. Mass Spectral and GC Data of Drugs, Poisons and their Metabolites. Parts I and II. Mass Spectra Indexes. Weinheim, FederalRepublic of Germany. 1985. 100]**PEER REVIEWED**

Surface Tension:

24 DYNES/CM AT 20 DEG C
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Vapor Density:

3.04 (AIR= 1)
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 641]**PEER REVIEWED**

Vapor Pressure:

Vapor pressure = 93.2 mm Hg at 25 deg C /from experimentally-derived coefficients/

[Daubert, T.E., R.P. Danner. Physical and Thermodynamic Properties of Pure Chemicals Data Compilation. Washington, D.C.: Taylor and Francis, 1989.]**PEER REVIEWED**

Viscosity:

0.44 CP at 25 deg C
[Weast, R.C. (ed.) Handbook of Chemistry and Physics. 69th ed. Boca Raton, FL: CRC Press Inc., 1988-1989.,p. F-42]**PEER REVIEWED**

Other Chemical/Physical Properties:

ACID VALUE NOT MORE THAN 0.01%
[Fenaroli's Handbook of Flavor Ingredients. Volume 2. Edited, translated, and revised by T.E. Furia and N. Bellanca. 2nd ed. Cleveland: The Chemical Rubber Co., 1975. 157]**PEER REVIEWED**

DISTILLS BETWEEN 76 & 77.5 DEG C
[Osol, A. (ed.). Remington's Pharmaceutical Sciences. 16th ed. Easton, Pennsylvania: Mack Publishing Co., 1980. 1232]**PEER REVIEWED**

DENSITY OF SATURATED AIR (AIR= 1) 1.02; CONVERSION FACTORS: 1 MG/L= 278 PPM; 1 PPM= 3.60 MG/CU M
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 22978]**PEER REVIEWED**

AZEOTROPIC MIXT WITH WATER (6.1% WT/WT), BP: 70.4 DEG C; AZEOTROPIC MIXT WITH WATER (7.8% WT/WT) & ALC (9.0% WT/WT) BP 70.3 DEG; ACQUIRES ACID REACTION WHEN DECOMP BY MOISTURE; ABSORBS WATER (UP TO 3.3% WT/WT)
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 641]**PEER REVIEWED**

LIQUID-WATER INTERFACIAL TENSION: 6.79 DYNES/CM AT 30 DEG C; VAPOR (GAS) SPECIFIC GRAVITY: 3.0; RATIO OF SPECIFIC HEATS OF VAPOR (GAS): 1.080
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Heat of fusion: 28.43 cal/g
[Weast, R.C. (ed.) Handbook of Chemistry and Physics. 69th ed. Boca Raton, FL: CRC Press Inc., 1988-1989.,p. C-667]**PEER REVIEWED**

Heat capacity: 167.4 J/mol K @ 1 atm
[Weast, R.C. (ed.) Handbook of Chemistry and Physics. 69th ed. Boca Raton, FL: CRC Press Inc., 1988-1989.,p. D-174]**PEER REVIEWED**

Henry's Law constant = 1.34X10-4 atm-cu m/mole at 25 deg C
[Butler JAV, Tamchandani CN; J Chem Soc: 952-5 (1935)]**PEER

REVIEWED**

More soluble (in water) at lower temps and less sol at higher temps.
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 641]**PEER REVIEWED**

ETHYL ACETATE

CASRN: 141-78-6

For other data, click on the Table of Contents

Molecular Formula:

C4-H8-O2

[The Merck Index. 10th ed. Rahway, New Jersey: Merck Co., Inc., 1983. 545]**PEER REVIEWED**

ETHYL ACETATE

CASRN: 141-78-6

For other data, click on the Table of Contents

Molecular Weight:

88.11

[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 641]**PEER REVIEWED**

ETHYL ACETATE

CASRN: 141-78-6

For other data, click on the Table of Contents

Color/Form:

CLEAR LIQUID

[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 641]**PEER REVIEWED**

Colorless liquid.

[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 94-116. Washington, D.C.: U.S. Government Printing Office, June 1994. 130]**PEER REVIEWED**

ETHYL ACETATE

CASRN: 141-78-6

For other data, click on the Table of Contents

Odor:

CHARACTERISTIC ETHER-LIKE ODOR REMINISCENT OF PINEAPPLE.
[Fenaroli's Handbook of Flavor Ingredients. Volume 2. Edited, translated, and revised by T.E. Furia and N. Bellanca. 2nd ed. Cleveland: The Chemical Rubber Co., 1975. 157]**PEER REVIEWED**

Fragrant odor
[Sax, N.I. Dangerous Properties of Industrial Materials. 6th ed. New York, NY: Van Nostrand Reinhold, 1984. 1315]**PEER REVIEWED**

Ether-like, fruity odor.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 94-116. Washington, D.C.: U.S. Government Printing Office, June 1994. 130]**PEER REVIEWED**

Fruity with a brandy note.
[Gerhartz, W. (exec ed.). Ullmann's Encyclopedia of Industrial Chemistry. 5th ed.Vol A1: Deerfield Beach, FL: VCH Publishers, 1985 to Present.,p. VA11 152]**PEER REVIEWED**

ETHYL ACETATE

CASRN: 141-78-6

For other data, click on the Table of Contents

Taste:

PLEASANT TASTE WHEN DILUTED.
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 641]**PEER REVIEWED**

BITTERSWEET, WINE-LIKE BURNING TASTE.
[Fenaroli's Handbook of Flavor Ingredients. Volume 2. Edited, translated, and revised by T.E. Furia and N. Bellanca. 2nd ed. Cleveland: The Chemical Rubber Co., 1975. 157]**PEER REVIEWED**

Ethyl acetate ... contributes a fruity flavor to beer.
[Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984.,p. 24 789 (1984)]**PEER REVIEWED**

ETHYL ACETATE

CASRN: 141-78-6

For other data, click on the Table of Contents

Boiling Point:

77 DEG C

[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 641]**PEER REVIEWED**

ETHYL ACETATE

CASRN: 141-78-6

For other data, click on the Table of Contents

Melting Point:

-83 DEG C

[Weast, R.C. (ed.) Handbook of Chemistry and Physics. 69th ed. Boca Raton, FL: CRC Press Inc., 1988-1989.,p. C-48]**PEER REVIEWED**

ETHYL ACETATE

CASRN: 141-78-6

For other data, click on the Table of Contents

Critical Temperature & Pressure:

Critical temperature: 250 DEG C; Critical pressure: 3.8 MN/SQ M

[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

ETHYL ACETATE

CASRN: 141-78-6

For other data, click on the Table of Contents

Density/Specific Gravity:

Sp gr: 0.902 AT 20 DEG C/4 DEG C

[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 641]**PEER REVIEWED**

ETHYL ACETATE

CASRN: 141-78-6

For other data, click on the Table of Contents

Heat of Combustion:

-5616 CAL/G

[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

ETHYL ACETATE

CASRN: 141-78-6

For other data, click on the Table of Contents

Heat of Vaporization:

87.6 CAL/G

[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

ETHYL ACETATE

CASRN: 141-78-6

For other data, click on the Table of Contents

Octanol/Water Partition Coefficient:

log Kow= 0.73

[Hansch, C., Leo, A., D. Hoekman. Exploring QSAR - Hydrophobic, Electronic, and Steric Constants. Washington, DC: American Chemical Society., 1995. 9]**PEER REVIEWED**

ETHYL ACETATE

CASRN: 141-78-6

For other data, click on the Table of Contents

Solubilities:

SOL IN ALCOHOL, ETHER, ACETONE, AND BENZENE

[Weast, R.C. (ed.) Handbook of Chemistry and Physics. 69th ed. Boca Raton, FL: CRC Press Inc., 1988-1989.,p. C-48]**PEER REVIEWED**

MISCIBLE WITH CHLOROFORM

[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 641]**PEER REVIEWED**

MISCIBLE IN FIXED & VOLATILE OILS.

[Osol, A. (ed.). Remington's Pharmaceutical Sciences. 16th ed. Easton, Pennsylvania: Mack Publishing Co., 1980. 1232]**PEER REVIEWED**

Very soluble in water (64 g/l at 25 deg C)

[Wasik SP et al; Octanol/Water Partition Coefficients and Aqueous Solubilities of Organic Compounds p.66 NBS TR81-2406 (1981)]**PEER REVIEWED**

Miscible with oxygenated and chlorinated solvents.

[Ashford, R.D. Ashford's Dictionary of Industrial Chemicals. London, England: Wavelength Publications Ltd., 1994. 387]**PEER REVIEWED**

In water, 8.01X10+4 mg/l at 25 deg C.

[Yalkowsky SH, Dannenfelser RM; Aquasol Database of Aqueous Solubility. Version 5. College of Pharmacy, Univ of Ariz - Tucson, AZ. PC Version (1992)]**PEER REVIEWED**

ETHYL ACETATE

CASRN: 141-78-6

For other data, click on the Table of Contents

Spectral Properties:

Index of Refraction = 1.3719 at 20 deg C/D

[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 641]**PEER REVIEWED**

MAX ABSORPTION (METHANOL): 209 NM (LOG E= 1.86); SADTLER REFERENCE NUMBER: 4 (IR, PRISM); 3 (IR, GRATING)

[Weast, R.C. (ed.). Handbook of Chemistry and Physics. 60th ed. Boca Raton, Florida: CRC Press Inc., 1979.,p. C-86]**PEER REVIEWED**

IR: 4802 (Coblentz Society Spectral Collection)

[Weast, R.C. and M.J. Astle. CRC Handbook of Data on Organic Compounds. Volumes I and II. Boca Raton, FL: CRC Press Inc. 1985.,p. V1 18]**PEER REVIEWED**

UV: 4-21 (Organic Electronic Spectral Data, Phillips et al, John Wiley & Sons, New York)

[Weast, R.C. and M.J. Astle. CRC Handbook of Data on Organic Compounds. Volumes I and II. Boca Raton, FL: CRC Press Inc. 1985.,p. V1 18]**PEER REVIEWED**

NMR: 79 (Varian Associates NMR Spectra Catalogue)

[Weast, R.C. and M.J. Astle. CRC Handbook of Data on Organic Compounds. Volumes I and II. Boca Raton, FL: CRC Press Inc. 1985.,p. V1 18]**PEER REVIEWED**

MASS: 158 (Atlas of Mass Spectral Data, John Wiley & Sons, New York)

[Weast, R.C. and M.J. Astle. CRC Handbook of Data on Organic Compounds. Volumes I and II. Boca Raton, FL: CRC Press Inc. 1985.,p. V1 18]**PEER REVIEWED**

Intense mass spectral peaks: 43 m/z, 61 m/z, 70 m/z, 73 m/z, 88 m/z

[Pfleger, K., H. Maurer and A. Weber. Mass Spectral and GC Data of Drugs, Poisons and their Metabolites. Parts I and II. Mass Spectra Indexes. Weinheim, FederalRepublic of Germany. 1985. 100]**PEER REVIEWED**

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For other data, click on the Table of Contents

Surface Tension:

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Vapor Density:

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ETHYL ACETATE

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Vapor pressure = 93.2 mm Hg at 25 deg C /from experimentally-derived coefficients/
[Daubert, T.E., R.P. Danner. Physical and Thermodynamic Properties of Pure Chemicals Data Compilation. Washington, D.C.: Taylor and Francis, 1989.]**PEER REVIEWED**

ETHYL ACETATE

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For other data, click on the Table of Contents

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CASRN: 141-78-6

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[Osol, A. (ed.). Remington's Pharmaceutical Sciences. 16th ed. Easton, Pennsylvania: Mack Publishing Co., 1980. 1232]**PEER REVIEWED**

DENSITY OF SATURATED AIR (AIR= 1) 1.02; CONVERSION FACTORS: 1 MG/L= 278 PPM; 1 PPM= 3.60 MG/CU M
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 22978]**PEER REVIEWED**

AZEOTROPIC MIXT WITH WATER (6.1% WT/WT), BP: 70.4 DEG C; AZEOTROPIC MIXT WITH WATER (7.8% WT/WT) & ALC (9.0% WT/WT) BP 70.3 DEG; ACQUIRES ACID REACTION WHEN DECOMP BY MOISTURE; ABSORBS WATER (UP TO 3.3% WT/WT)
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 641]**PEER REVIEWED**

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[Weast, R.C. (ed.) Handbook of Chemistry and Physics. 69th ed. Boca Raton, FL: CRC Press Inc., 1988-1989.,p. D-174]**PEER REVIEWED**

Henry's Law constant = 1.34X10-4 atm-cu m/mole at 25 deg C
[Butler JAV, Tamchandani CN; J Chem Soc: 952-5 (1935)]**PEER REVIEWED**

More soluble (in water) at lower temps and less sol at higher temps.
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc.,

1996. 641]**PEER REVIEWED**

ETHYL ACETATE

CASRN: 141-78-6

For other data, click on the Table of Contents

Chemical Safety & Handling:

DOT Emergency Guidelines:

Fire or explosion: Highly flammable: Will be easily ignited by heat, sparks or flames. Vapors may form explosive mixtures with air. Vapors may travel to source of ignition and flash back. Most vapors are heavier than air. They will spread along ground and collect in low confined areas (sewers, basements, tanks). Vapor explosion hazard indoors, outdoors or in sewers. Some may polymerize (P) explosively when heated or involved in a fire. Runoff to sewer may create fire or explosion hazard. Containers may explode when heated. Many liquids are lighter than water.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

Health: May cause toxic effects if inhaled or absorbed through skin. Inhalation or contact with material may irritate or burn skin and eyes. Fire will produce irritating, corrosive and/or toxic gases. Vapors may cause dizziness or suffocation. Runoff from fire control or dilution water may cause pollution.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

Public safety: Call Emergency Response Telephone Number. ... Isolate spill or leak area immediately for at least 50 to lOO meters (160 to 330 feet) in all directions. Keep unauthorized personnel away. Stay upwind. Keep out of low areas. Ventilate closed spaces before entering.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

Protective clothing: Wear positive pressure self-contained breathing apparatus (SCBA). Structural firefighters' protective clothing will only provide limited protection.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs

Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

Evacuation: Large spill: Consider initial downwind evacuation for at least 300 meters (1000 feet). Fire: If tank, rail car or tank truck is involved in a fire, isolate for 800 meters (1/2 mile) in all directions; also, consider initial evacuation for 800 meters (1/2 mile) in all directions.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

Fire: Caution: All these products have a very low flash point: Use of water spray when fighting fire may be inefficient. Small fires: Dry chemical, CO2, water spray or alcohol-resistant foam. ... Large fires: Water spray, fog or alcohol-resistant foam. Do not use straight streams. Move containers from fire area if you can do it without risk. Fire involving tanks or car/trailer loads: Fight fire from maximum distance or use unmanned hose holders or monitor nozzles. Cool containers with flooding quantities of water until well after fire is out. Withdraw immediately in case of rising sound from venting safety devices or discoloration of tank. Always stay away from the ends of tanks. For massive fire, use unmanned hose holders or monitor nozzles; if this is impossible, withdraw from area and let fire burn.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

Spill or leak: Eliminate all ignition sources (no smoking, flares, sparks or flames in immediate area). All equipment used when handling the product must be grounded. Do not touch or walk through spilled material. Stop leak if you can do it without risk. Prevent entry into waterways, sewers, basements or confined areas. A vapor suppressing foam may be used to reduce vapors. Absorb or cover with dry earth, sand or other non-combustible material and transfer to containers. Use clean non-sparking tools to collect absorbed material. Large spills: Dike far ahead of liquid spill for later disposal. Water spray may reduce vapor; but may not prevent ignition in closed spaces.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

First aid: Move victim to fresh air. Call emergency medical care. Apply artificial respiration if victim is not breathing. Administer oxygen if breathing is difficult. Remove and isolate contaminated clothing and shoes. In case of contact with substance, immediately flush skin or eyes with running water for at least 20 minutes. Wash skin with soap and water. Keep victim warm and quiet. Effects of exposure (inhalation, ingestion or skin contact) to substance may be delayed. Ensure that medical personnel are aware of the

material(s) involved, and take precautions to protect themselves.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

Odor Threshold:

DETECTION IN AIR IS 0.006 TO 0.686 MG/L; DETECTION IN WATER IS 5 PPM.
[Clayton, G. D. and F. E. Clayton (eds.). Patty's Industrial Hygiene and Toxicology: Volume 2A, 2B, 2C: Toxicology. 3rd ed. New York: John Wiley Sons, 1981-1982. 2276]**PEER REVIEWED**

Detection in air: 3.6-1.120 mg cu/m
[Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984.,p. V10 460 (1980)]**PEER REVIEWED**

0.0196 mg/cu m (low odor); 665.0 mg/cu m (high odor); 350 mg/cu m (irritating concn)
[Ruth JH; Am Ind Hyg Assoc J 47: A-142-51 (1986)]**PEER REVIEWED**

Skin, Eye and Respiratory Irritations:

Irritating to mucous surfaces, particularly the eyes, gums and respiratory passages ... . On repeated or prolonged exposures, it causes conjunctival irritation and corneal clouding.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1514]**PEER REVIEWED**

Fire Potential:

DANGEROUS WHEN EXPOSED TO HEAT OR FLAME
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1514]**PEER REVIEWED**

NFPA Hazard Classification:

Health: 1. 1= Materials that, on exposure, would cause irritation, but only minor residual injury, including those requiring the use of an approved air-purifying respirator. These materials are only slightly hazardous to health and only breathing protection is needed.
[National Fire Protection Guide. Fire Protection Guide on Hazardous Materials. 10 th ed. Quincy, MA: National Fire Protection Association, 1991.,p. 325M-47]**PEER REVIEWED**

Flammability: 3. 3= Includes Class IB and IC flammable liquids and materials that can be easily ignited under almost all normal temperature conditions. Water may be ineffective in controlling or extinguishing fires in such materials.

[National Fire Protection Guide. Fire Protection Guide on Hazardous Materials. 10 th ed. Quincy, MA: National Fire Protection Association, 1991.,p. 325M-47]**PEER REVIEWED**

Reactivity: 0. 0= Includes materials that are normally stable, even under fire exposure conditions, and that do not react with water. Normal fire fighting procedures may be used.
[National Fire Protection Guide. Fire Protection Guide on Hazardous Materials. 10 th ed. Quincy, MA: National Fire Protection Association, 1991.,p. 325M-47]**PEER REVIEWED**

Flammable Limits:

LOWER 2.2%; UPPER 9%
[American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices. 5th ed. Cincinnati, OH:American Conference of Governmental Industrial Hygienists, 1986. 239]**PEER REVIEWED**

Flash Point:

7.2 DEG C (OPEN CUP)
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 3806]**PEER REVIEWED**

Autoignition Temperature:

800 DEG F
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 3806]**PEER REVIEWED**

Fire Fighting Procedures:

COOL EXPOSED CONTAINERS WITH WATER.
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

/USE/ CARBON DIOXIDE, DRY CHEM, OR ALCOHOL FOAM.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1514]**PEER REVIEWED**

If material on fire or involved in fire: Do not extinguish fire unless flow can be stopped or safely confined. Use water in flooding quantities as fog. Solid streams of water may be ineffective. Apply water from as far a distance as possible. Cool all affected containers with flooding quantities of water. Use "alcohol" foam, dry chemical or carbon dioxide.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of

American Railroads, Bureau of Explosives, 1994. 439]**PEER REVIEWED**

Firefighting Hazards:

FLASHBACK ALONG VAPOR TRAIL MAY OCCUR.
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Explosive Limits & Potential:

THE LIQUID ... PRODUCES A VAPOR THAT FORMS EXPLOSIVE MIXTURES WITH AIR AT NORMAL TEMPERATURES.
[International Labour Office. Encyclopedia of Occupational Health and Safety. Volumes I and II. New York: McGraw-Hill Book Co., 1971. 477]**PEER REVIEWED**

Explosive limits mol fraction in air: Upper 0.090, Lower 0.025
[Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984.,p. V21 369 (1983)]**PEER REVIEWED**

Hazardous Reactivities & Incompatibilities:

... CAN REACT VIGOROUSLY WITH CHLOROSULFONIC ACID, ... OLEUM, K-TERT-BUTOXIDE ...Explosive reaction with lithium tetrahydroaluminate.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1514]**PEER REVIEWED**

Incompatible with nitrates, strong oxidizers, strong alkalies, strong acids.
[Sittig, M. Handbook of Toxic and Hazardous Chemicals and Carcinogens, 1985. 2nd ed. Park Ridge, NJ: Noyes Data Corporation, 1985. 408]**PEER REVIEWED**

Nitrates, strong oxidizers, alkalis & acids.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 130]**QC REVIEWED**

Hazardous Decomposition:

When heated to decomposition it emits acrid smoke and irritating fumes.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1514]**PEER REVIEWED**

On storage, it is slowly decomposed by water.
[Snyder, R. (ed.). Ethel Browning's Toxicity and Metabolism of Industrial Solvents. Second Edition. Volume 3 Alcohols and Esters. New

York, NY: Elsevier, 1992. 234]**PEER REVIEWED**

Prior History of Accidents:

The wreck of the MV Ariadne, a Panamanian flag container ship, is examined as a case study of a hazardous substance emergency response in a third world country. /The ship/, carrying a cargo of heavy fuel oil, tetraethyl lead, xylene, toluene, methyl isobutyl ketone, butyl acetate, **ethyl acetate,** and acetone was grounded while departing the harbor of Mogadishu, Somalia. The Somalian government requested a team of technical advisors to help respond appropriately to the emergency. The major issues addressed by the advisory team were the need for additional salvage equipment and expertise, the danger of toxic fumes from the fire and explosions aboard the ship, the presence and possible release of tetraethyl lead, possible port blockage by the wreck, recovery of the chemical drums, and the extent of environmental damage caused by the release of oil, pesticides, and tetraethyl lead into the harbor. ...
[Heare SF et al; 1986 Hazard Matl Spill Conf p.12-18 (1986)]**PEER REVIEWED**

Immediately Dangerous to Life or Health:

2000 ppm (Based on 10% of the lower explosive limit for safety considerations even though the relevant toxicological data indicated that irreversible health effects or impairment of escape existed only at higher concentrations.)
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 130]**QC REVIEWED**

Protective Equipment & Clothing:

ORGANIC VAPOR CANISTER OR AIR MASK; GOGGLES OR FACE SHIELD.
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Wear appropriate clothing to prevent repeated or prolonged skin contact.
[Sittig, M. Handbook of Toxic and Hazardous Chemicals and Carcinogens, 1985. 2nd ed. Park Ridge, NJ: Noyes Data Corporation, 1985. 409]**PEER REVIEWED**

Breakthrough times greater than one hour reported by (normally) two or more testers for butyl rubber (Butyl). Some data usually from immersion tests suggesting breakthrough times greater than one hour are not likely for natural rubber (Nat Rub), polyethylene (PE) and polyvinyl alcohol (PVA). Breakthrough times less (usually significantly less) than one hour reported by (normally) two or more testers for neoprene (Neop), nitrile rubber (nitrile), and polyvinyl chloride (PVC). No data for neoprene /styrene-butadiene rubber (Neop/ SBR), nitrile rubber/polyvinyl chloride (Nitrile/PVC), chlorinated polyethylene (CPE), polyurethane (PU), styrene-butadiene rubber (SBR) and viton.
[ACGIH; Guidelines Select of Chem Protect Clothing Volume #1 Field Guide p.44 (1983)]**PEER REVIEWED**

Wear appropriate personal protective clothing to prevent skin contact.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH)

Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 131]**QC REVIEWED**

Wear appropriate eye protection to prevent eye contact.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 131]**QC REVIEWED**

Recommendations for respirator selection. Max concn for use: 2000 ppm. Respirator Class(es): Any supplied-air respirator operated in a continuous flow mode. Eye protection needed. Any powered, air-purifying respirator with organic vapor cartridge(s). Eye protection needed. Any chemical cartridge respirator with a full facepiece and organic vapor cartridge(s). Any air-purifying, full-facepiece respirator (gas mask) with a chin-style, front- or back-mounted organic vapor canister. Any self-contained breathing apparatus with a full facepiece. Any supplied-air respirator with a full facepiece.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 131]**QC REVIEWED**

Recommendations for respirator selection. Condition: Emergency or planned entry into unknown concn or IDLH conditions: Respirator Class(es): Any self-contained breathing apparatus that has a full facepiece and is operated in a pressure-demand or other positive-pressure mode. Any supplied-air respirator that has a full facepiece and is operated in a pressure-demand or other positive-pressure mode in combination with an auxiliary self-contained breathing apparatus operated in pressure-demand or other positive-pressure mode.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 131]**QC REVIEWED**

Recommendations for respirator selection. Condition: Escape from suddenly occurring respiratory hazards: Respirator Class(es): Any air-purifying, full-facepiece respirator (gas mask) with a chin-style, front- or back-mounted organic vapor canister. Any appropriate escape-type, self-contained breathing apparatus.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 131]**QC REVIEWED**

Wear positive-pressure SCBA and protective equipment ... . If special chemical protective clothing is required, consult the chemical manufacturer or specific protective clothing compatibility charts. Delay entry until trained personnel and proper protective equipment are available. Remove patient from contaminated area. Quickly remove and isolate patient's clothing, jewelry, and shoes. Gently blot excess liquids with absorbent material. Rinse patient with warm water, 30 deg C/86 deg F, if possible. Wash patient with Tincture of Green Soap or a mild liquid soap and large quantities of water.
[Bronstein, A.C., P.L. Currance; Emergency Care for Hazardous Materials Exposure. 2nd ed. St. Louis, MO. Mosby Lifeline. 1994. 221]**PEER REVIEWED**

SRP: Contaminated protective clothing should be segregated in such a manner so that there is no direct personal contact by personnel who handle, dispose, or clean the clothing. Quality assurance to ascertain

the completeness of the cleaning procedures should be implemented before the decontaminated protective clothing is returned for reuse by the workers. Contaminated clothing should not be taken home at end of shift, but should remain at employee's place of work for cleaning.
PEER REVIEWED

Preventive Measures:

USE EFFECTIVE FUME REMOVAL DEVICE /IN LABORATORY/.
[Association of Official Analytical Chemists. Official Methods of Analysis. 10th ed. and supplements. Washington, DC: Association of Official Analytical Chemists, 1965. New editions through13th ed. plus supplements, 1982.,p. 13/882 51.057]**PEER REVIEWED**

Employees should wash promptly when skin is wet or contaminated. Remove clothing immediately if wet or contaminated to avoid flammability hazard.
[Sittig, M. Handbook of Toxic and Hazardous Chemicals and Carcinogens, 1985. 2nd ed. Park Ridge, NJ: Noyes Data Corporation, 1985. 409]**PEER REVIEWED**

Avoid breathing vapors. Keep upwind. Wear appropriate chemical protective gloves, boots and goggles. Do not handle broken packages unless wearing appropriate personal protective equipment. Wash away any material which may have contacted the body with copious amounts of water or soap and water.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 439]**PEER REVIEWED**

Contact lenses should not be worn when working with this chemical.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 131]**QC REVIEWED**

SRP: The scientific literature for the use of contact lenses in industry is conflicting. The benefit or detrimental effects of wearing contact lenses depend not only upon the substance, but also on factors including the form of the substance, characteristics and duration of the exposure, the uses of other eye protection equipment, and the hygiene of the lenses. However, there may be individual substances whose irritating or corrosive properties are such that the wearing of contact lenses would be harmful to the eye. In those specific cases, contact lenses should not be worn. In any event, the usual eye protection equipment should be worn even when contact lenses are in place.
PEER REVIEWED

If material not on fire and not involved in fire: Keep sparks, flames and other sources of ignition away. Keep material out of water sources and sewers. Build dikes to contain flow as necessary. Attempt to stop leak if without undue personnel hazard. Use water spray to disperse vapors and dilute standing pools of liquid.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 439]**PEER REVIEWED**

SRP: Contaminated protective clothing should be segregated in such a manner so that there is no direct

personal contact by personnel who handle, dispose, or clean the clothing. Quality assurance to ascertain the completeness of the cleaning procedures should be implemented before the decontaminated protective clothing is returned for reuse by the workers. Contaminated clothing should not be taken home at end of shift, but should remain at employee's place of work for cleaning.
PEER REVIEWED

The worker should immediately wash the skin when it becomes contaminated.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 131]**QC REVIEWED**

Work clothing that becomes wet should be immediately removed due to its flammability hazard.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 131]**QC REVIEWED**

An analysis of breakthrough times of low boiling organic solvent vapors in a commercial respirator cartridge under steady state and pulsating flow conditions was performed. A KGC-8 respirator cartridge packed with 22.5 grams of activated charcoal was exposed to 0, 100, 300, or 900 ppm carbon-tetrachloride, **ethyl-acetate,** methyl-acetate, acetone, or dichloromethane vapor under steady state or pulsed flow conditions in custom built apparatus. The steady state flow condition was achieved by setting the respirator cartridge in its holder and passing each solvent vapor through it at a flow rate of 30 liter per minute (l/min). The pulsating flow condition was achieved placing the respirator cartridge in a Tedler bag, expanding the bag by introducing each test vapor, and 'inhaling' the test vapor through the respirator cartridge using a breathing machine drawing 1.5 liters air per cycle at the rate 20 cycles/min. The total flow rate was adjusted to be similar to the 301/min rate utilized the steady state flow experiments. Solvent vapor concentrations were measured upstream and downstream from the cartridge by gas chromatography. Breakthrough times were determined as the time required for the solvent vapor concentrations downstream from the cartridge to increase to 5 ppm. The data were analyzed by logistic regression techniques. After converting the data to logarithms, the breakthrough times of all five solvents were linearly, inversely proportional to their initial concentrations under both steady state and pulsed flow conditions. The slopes of the lines were smaller for the solvents with the lower boiling points. The ratios of the breakthrough times measured under the pulsating flow to the steady slate flow condition (B/A ratio) varied from 0.77 to 0.71 for dichloromethane. The B/A ratios for the lOO ppm initial concentrations of the other four solvents varied only from 0.95 to 1.01. This indicated that except in the case of dichloromethane, there are no large differences in breakthrough tire under the two different flow conditions at lOO ppm. At the other concentrations, in each experiment as the concentration of the test vapor increased the breakthrough times under the pulsating flow condition became shorter compared to the steady state flow condition. /It was/ concluded that breakthrough of low boiling solvent vapors in respirator cartridges occurs earlier under pulsating flow than under steady state conditions.
[Tanaka S et al; Industrial Health 34 (2): 125-31 (1996)]**PEER REVIEWED**

Stability/Shelf Life:

SLOWLY DECOMP BY MOISTURE.
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals,

Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 3806]**PEER REVIEWED**

Shipment Methods and Regulations:

No person may /transport,/ offer or accept a hazardous material for transportation in commerce unless that person is registered in conformance ... and the hazardous material is properly classed, described, packaged, marked, labeled, and in condition for shipment as required or authorized by ... /the hazardous materials regulations (49 CFR 171-177)./
[49 CFR 171.2 (7/1/96)]**PEER REVIEWED**

The International Air Transport Association (IATA) Dangerous Goods Regulations are published by the IATA Dangerous Goods Board pursuant to IATA Resolutions 618 and 619 and constitute a manual of industry carrier regulations to be followed by all IATA Member airlines when transporting hazardous materials.
[IATA. Dangerous Goods Regulations. 38th ed. Montreal, Canada and Geneva, Switzerland: International Air Transport Association, Dangerous Goods Board, January, 1997. 146]**PEER REVIEWED**

The International Maritime Dangerous Goods Code lays down basic principles for transporting hazardous chemicals. Detailed recommendations for individual substances and a number of recommendations for good practice are included in the classes dealing with such substances. A general index of technical names has also been compiled. This index should always be consulted when attempting to locate the appropriate procedures to be used when shipping any substance or article.
[IMDG; International Maritime Dangerous Goods Code; International Maritime Organization p.3075 (1988)]**PEER REVIEWED**

Storage Conditions:

KEEP TIGHTLY CLOSED IN COOL PLACE & AWAY FROM FIRE.
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 3806]**PEER REVIEWED**

DURING TRANSPORT: STABLE DURING TRANSPORT. STORAGE TEMPERATURE: AMBIENT. VENTING: OPEN (FLAME ARRESTER) OR PRESSURE-VACUUM.
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

On storage, it is slowly decomposed by water.
[Snyder, R. (ed.). Ethel Browning's Toxicity and Metabolism of Industrial Solvents. Second Edition. Volume 3 Alcohols and Esters. New York, NY: Elsevier, 1992. 234]**PEER REVIEWED**

Cleanup Methods:

1. REMOVE ALL IGNITION SOURCES. 2. VENTILATE AREA OF SPILL OR LEAK. 3. FOR SMALL QUANTITIES, ABSORB ON PAPER TOWELS. EVAPORATE IN A SAFE PLACE (SUCH

AS A FUME HOOD). ALLOW SUFFICIENT TIME FOR EVAPORATING VAPORS TO COMPLETELY CLEAR THE HOOD DUCTWORK. BURN THE PAPER IN A SUITABLE LOCATION AWAY FROM COMBUSTIBLE MATERIALS. LARGE QUANTITIES CAN BE COLLECTED AND ATOMIZED IN A SUITABLE COMBUSTION CHAMBER. **ETHYL ACETATE** SHOULD NOT BE ALLOWED TO ENTER A CONFINED SPACE, SUCH AS A SEWER, BECAUSE OF THE POSSIBILITY OF AN EXPLOSION.
[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) PublicationNo. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981. 3]**PEER REVIEWED**

Disposal Methods:

Generators of waste (equal to or greater than 100 kg/mo) containing this contaminant, EPA hazardous waste numbers U112 and F003, must conform with USEPA regulations in storage, transportation, treatment and disposal of waste.
[40 CFR 240-280, 300-306, 702-799 (7/1/89)]**PEER REVIEWED**

Incineration: Burn waste material in an approved waste disposal incinerator.
[United Nations. Treatment and Disposal Methods for Waste Chemicals (IRPTC File). Data Profile Series No. 5. Geneva, Switzerland: United Nations Environmental Programme, Dec. 1985. 72]**PEER REVIEWED**

1. BY ABSORBING IT IN VERMICULITE, DRY SAND, EARTH, OR A SIMILAR MATERIAL. 2. BY ATOMIZING IN A SUITABLE COMBUSTION CHAMBER.
[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) PublicationNo. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981. 3]**PEER REVIEWED**

Ethyl acetate is a waste chemical stream constituent which may be subjected to ultimate disposal by controlled incineration.
[USEPA; Engineering Handbook for Hazardous Waste Incineration p.2-6 (1981) EPA 68-03-3025]**PEER REVIEWED**

A good candidate for rotary kiln incineration at a temperature range of 820 to 1,600 deg C and residence times of seconds for liquids and gases, and hours for solids. A good candidate for liquid injection incineration at a temperature range of 650 to 1,600 deg C and a residence time of 0.1 to 2 seconds. A good candidate for fluidized bed incineration at a temperature range of 450 to 980 deg C and residence times of seconds for liquids and gases, and longer for solids.
[USEPA; Engineering Handbook for Hazardous Waste Incineration p.3-13 (1981) EPA 68-03-3025]**PEER REVIEWED**

The following wastewater treatment technologies have been investigated for **Ethyl acetate:**
Concentration process: Biological treatment.
[USEPA; Management of Hazardous Waste Leachate, EPA Contract No.68-03-2766 p.E-33 (1982)]**PEER REVIEWED**

The following wastewater treatment technologies have been investigated for **Ethyl acetate:**

Concentration process: Activated carbon.
[USEPA; Management of Hazardous Waste Leachate, EPA Contract No.68-03-2766 p.E-133 (1982)]**PEER REVIEWED**

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DOT Emergency Guidelines:

Fire or explosion: Highly flammable: Will be easily ignited by heat, sparks or flames. Vapors may form explosive mixtures with air. Vapors may travel to source of ignition and flash back. Most vapors are heavier than air. They will spread along ground and collect in low confined areas (sewers, basements, tanks). Vapor explosion hazard indoors, outdoors or in sewers. Some may polymerize (P) explosively when heated or involved in a fire. Runoff to sewer may create fire or explosion hazard. Containers may explode when heated. Many liquids are lighter than water.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

Health: May cause toxic effects if inhaled or absorbed through skin. Inhalation or contact with material may irritate or burn skin and eyes. Fire will produce irritating, corrosive and/or toxic gases. Vapors may cause dizziness or suffocation. Runoff from fire control or dilution water may cause pollution.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

Public safety: Call Emergency Response Telephone Number. ... Isolate spill or leak area immediately for at least 50 to lOO meters (160 to 330 feet) in all directions. Keep unauthorized personnel away. Stay upwind. Keep out of low areas. Ventilate closed spaces before entering.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

Protective clothing: Wear positive pressure self-contained breathing apparatus (SCBA). Structural firefighters' protective clothing will only provide limited protection.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

Evacuation: Large spill: Consider initial downwind evacuation for at least 300 meters (1000 feet). Fire: If tank, rail car or tank truck is involved in a fire, isolate for 800 meters (1/2 mile) in all directions; also, consider initial evacuation for 800 meters (1/2 mile) in all directions.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

Fire: Caution: All these products have a very low flash point: Use of water spray when fighting fire may be inefficient. Small fires: Dry chemical, CO2, water spray or alcohol-resistant foam. ... Large fires: Water spray, fog or alcohol-resistant foam. Do not use straight streams. Move containers from fire area if you can do it without risk. Fire involving tanks or car/trailer loads: Fight fire from maximum distance or use unmanned hose holders or monitor nozzles. Cool containers with flooding quantities of water until well after fire is out. Withdraw immediately in case of rising sound from venting safety devices or discoloration of tank. Always stay away from the ends of tanks. For massive fire, use unmanned hose holders or monitor nozzles; if this is impossible, withdraw from area and let fire burn.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

Spill or leak: Eliminate all ignition sources (no smoking, flares, sparks or flames in immediate area). All equipment used when handling the product must be grounded. Do not touch or walk through spilled material. Stop leak if you can do it without risk. Prevent entry into waterways, sewers, basements or confined areas. A vapor suppressing foam may be used to reduce vapors. Absorb or cover with dry earth, sand or other non-combustible material and transfer to containers. Use clean non-sparking tools to collect absorbed material. Large spills: Dike far ahead of liquid spill for later disposal. Water spray may reduce vapor; but may not prevent ignition in closed spaces.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

First aid: Move victim to fresh air. Call emergency medical care. Apply artificial respiration if victim is not breathing. Administer oxygen if breathing is difficult. Remove and isolate contaminated clothing and shoes. In case of contact with substance, immediately flush skin or eyes with running water for at least 20 minutes. Wash skin with soap and water. Keep victim warm and quiet. Effects of exposure (inhalation, ingestion or skin contact) to substance may be delayed. Ensure that medical personnel are aware of the material(s) involved, and take precautions to protect themselves.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the

Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

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Odor Threshold:

DETECTION IN AIR IS 0.006 TO 0.686 MG/L; DETECTION IN WATER IS 5 PPM.
[Clayton, G. D. and F. E. Clayton (eds.). Patty's Industrial Hygiene and Toxicology: Volume 2A, 2B, 2C: Toxicology. 3rd ed. New York: John Wiley Sons, 1981-1982. 2276]**PEER REVIEWED**

Detection in air: 3.6-1.120 mg cu/m
[Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984.,p. V10 460 (1980)]**PEER REVIEWED**

0.0196 mg/cu m (low odor); 665.0 mg/cu m (high odor); 350 mg/cu m (irritating concn)
[Ruth JH; Am Ind Hyg Assoc J 47: A-142-51 (1986)]**PEER REVIEWED**

ETHYL ACETATE

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For other data, click on the Table of Contents

Fire Potential:

DANGEROUS WHEN EXPOSED TO HEAT OR FLAME

[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1514]**PEER REVIEWED**

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NFPA Hazard Classification:

Health: 1. 1= Materials that, on exposure, would cause irritation, but only minor residual injury, including those requiring the use of an approved air-purifying respirator. These materials are only slightly hazardous to health and only breathing protection is needed.
[National Fire Protection Guide. Fire Protection Guide on Hazardous Materials. 10 th ed. Quincy, MA: National Fire Protection Association, 1991.,p. 325M-47]**PEER REVIEWED**

Flammability: 3. 3= Includes Class IB and IC flammable liquids and materials that can be easily ignited under almost all normal temperature conditions. Water may be ineffective in controlling or extinguishing fires in such materials.
[National Fire Protection Guide. Fire Protection Guide on Hazardous Materials. 10 th ed. Quincy, MA: National Fire Protection Association, 1991.,p. 325M-47]**PEER REVIEWED**

Reactivity: 0. 0= Includes materials that are normally stable, even under fire exposure conditions, and that do not react with water. Normal fire fighting procedures may be used.
[National Fire Protection Guide. Fire Protection Guide on Hazardous Materials. 10 th ed. Quincy, MA: National Fire Protection Association, 1991.,p. 325M-47]**PEER REVIEWED**

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Flammable Limits:

LOWER 2.2%; UPPER 9%

[American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices. 5th ed. Cincinnati, OH:American Conference of Governmental Industrial Hygienists, 1986. 239]**PEER REVIEWED**

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For other data, click on the Table of Contents

Flash Point:

7.2 DEG C (OPEN CUP)

[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 3806]**PEER REVIEWED**

ETHYL ACETATE

CASRN: 141-78-6

For other data, click on the Table of Contents

Autoignition Temperature:

800 DEG F

[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 3806]**PEER REVIEWED**

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For other data, click on the Table of Contents

Fire Fighting Procedures:

COOL EXPOSED CONTAINERS WITH WATER.
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

/USE/ CARBON DIOXIDE, DRY CHEM, OR ALCOHOL FOAM.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1514]**PEER REVIEWED**

If material on fire or involved in fire: Do not extinguish fire unless flow can be stopped or safely confined. Use water in flooding quantities as fog. Solid streams of water may be ineffective. Apply water from as far a distance as possible. Cool all affected containers with flooding quantities of water. Use "alcohol" foam, dry chemical or carbon dioxide.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 439]**PEER REVIEWED**

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For other data, click on the Table of Contents

Firefighting Hazards:

FLASHBACK ALONG VAPOR TRAIL MAY OCCUR.

[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

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Explosive Limits & Potential:

THE LIQUID ... PRODUCES A VAPOR THAT FORMS EXPLOSIVE MIXTURES WITH AIR AT NORMAL TEMPERATURES.
[International Labour Office. Encyclopedia of Occupational Health and Safety. Volumes I and II. New York: McGraw-Hill Book Co., 1971. 477]**PEER REVIEWED**

Explosive limits mol fraction in air: Upper 0.090, Lower 0.025
[Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984.,p. V21 369 (1983)]**PEER REVIEWED**

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Hazardous Reactivities & Incompatibilities:

... CAN REACT VIGOROUSLY WITH CHLOROSULFONIC ACID, ... OLEUM, K-TERT-BUTOXIDE ...Explosive reaction with lithium tetrahydroaluminate.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1514]**PEER REVIEWED**

Incompatible with nitrates, strong oxidizers, strong alkalies, strong acids.
[Sittig, M. Handbook of Toxic and Hazardous Chemicals and Carcinogens, 1985. 2nd ed. Park Ridge, NJ: Noyes Data Corporation, 1985. 408]**PEER REVIEWED**

Nitrates, strong oxidizers, alkalis & acids.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 130]**QC REVIEWED**

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Hazardous Decomposition:

When heated to decomposition it emits acrid smoke and irritating fumes.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1514]**PEER REVIEWED**

On storage, it is slowly decomposed by water.
[Snyder, R. (ed.). Ethel Browning's Toxicity and Metabolism of Industrial Solvents. Second Edition. Volume 3 Alcohols and Esters. New York, NY: Elsevier, 1992. 234]**PEER REVIEWED**

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Prior History of Accidents:

The wreck of the MV Ariadne, a Panamanian flag container ship, is examined as a case study of a hazardous substance emergency response in a third world country. /The ship/, carrying a cargo of heavy fuel oil, tetraethyl lead, xylene, toluene, methyl isobutyl ketone, butyl acetate, **ethyl acetate,** and acetone was grounded while departing the harbor of Mogadishu, Somalia. The Somalian government requested a team of technical advisors to help respond appropriately to the emergency. The major issues addressed by the advisory team were the need for additional salvage equipment and expertise, the danger of toxic fumes from the fire and explosions aboard the ship, the presence and possible release of tetraethyl lead, possible port blockage by the wreck, recovery of the chemical drums, and the extent of environmental damage caused by the release of oil, pesticides, and tetraethyl lead into the harbor. ...
[Heare SF et al; 1986 Hazard Matl Spill Conf p.12-18 (1986)]**PEER REVIEWED**

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Immediately Dangerous to Life or Health:

2000 ppm (Based on 10% of the lower explosive limit for safety considerations even though the relevant toxicological data indicated that irreversible health effects or impairment of escape existed only at higher concentrations.)

[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 130]**QC REVIEWED**

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Protective Equipment & Clothing:

ORGANIC VAPOR CANISTER OR AIR MASK; GOGGLES OR FACE SHIELD.
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Wear appropriate clothing to prevent repeated or prolonged skin contact.
[Sittig, M. Handbook of Toxic and Hazardous Chemicals and Carcinogens, 1985. 2nd ed. Park Ridge, NJ: Noyes Data Corporation, 1985. 409]**PEER REVIEWED**

Breakthrough times greater than one hour reported by (normally) two or more testers for butyl rubber (Butyl). Some data usually from immersion tests suggesting breakthrough times greater than one hour are not likely for natural rubber (Nat Rub), polyethylene (PE) and polyvinyl alcohol (PVA). Breakthrough times less (usually significantly less) than one hour reported by (normally) two or more testers for neoprene (Neop), nitrile rubber (nitrile), and polyvinyl chloride (PVC). No data for neoprene /styrene-butadiene rubber (Neop/ SBR), nitrile rubber/polyvinyl chloride (Nitrile/PVC), chlorinated polyethylene (CPE), polyurethane (PU), styrene-butadiene rubber (SBR) and viton.
[ACGIH; Guidelines Select of Chem Protect Clothing Volume #1 Field Guide p.44 (1983)]**PEER REVIEWED**

Wear appropriate personal protective clothing to prevent skin contact.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 131]**QC REVIEWED**

Wear appropriate eye protection to prevent eye contact.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 131]**QC REVIEWED**

Recommendations for respirator selection. Max concn for use: 2000 ppm. Respirator Class(es): Any supplied-air respirator operated in a continuous flow mode. Eye protection needed. Any powered, air-purifying respirator with organic vapor cartridge(s). Eye protection needed. Any chemical cartridge respirator with a full facepiece and organic vapor cartridge(s). Any air-purifying, full-facepiece respirator (gas mask) with a chin-style, front- or back-mounted organic vapor canister. Any self-contained breathing apparatus with a full facepiece. Any supplied-air respirator with a full facepiece.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 131]**QC REVIEWED**

Recommendations for respirator selection. Condition: Emergency or planned entry into unknown concn or IDLH conditions: Respirator Class(es): Any self-contained breathing apparatus that has a full

facepiece and is operated in a pressure-demand or other positive-pressure mode. Any supplied-air respirator that has a full facepiece and is operated in a pressure-demand or other positive-pressure mode in combination with an auxiliary self-contained breathing apparatus operated in pressure-demand or other positive-pressure mode.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 131]**QC REVIEWED**

Recommendations for respirator selection. Condition: Escape from suddenly occurring respiratory hazards: Respirator Class(es): Any air-purifying, full-facepiece respirator (gas mask) with a chin-style, front- or back-mounted organic vapor canister. Any appropriate escape-type, self-contained breathing apparatus.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 131]**QC REVIEWED**

Wear positive-pressure SCBA and protective equipment ... . If special chemical protective clothing is required, consult the chemical manufacturer or specific protective clothing compatibility charts. Delay entry until trained personnel and proper protective equipment are available. Remove patient from contaminated area. Quickly remove and isolate patient's clothing, jewelry, and shoes. Gently blot excess liquids with absorbent material. Rinse patient with warm water, 30 deg C/86 deg F, if possible. Wash patient with Tincture of Green Soap or a mild liquid soap and large quantities of water.
[Bronstein, A.C., P.L. Currance; Emergency Care for Hazardous Materials Exposure. 2nd ed. St. Louis, MO. Mosby Lifeline. 1994. 221]**PEER REVIEWED**

SRP: Contaminated protective clothing should be segregated in such a manner so that there is no direct personal contact by personnel who handle, dispose, or clean the clothing. Quality assurance to ascertain the completeness of the cleaning procedures should be implemented before the decontaminated protective clothing is returned for reuse by the workers. Contaminated clothing should not be taken home at end of shift, but should remain at employee's place of work for cleaning.
PEER REVIEWED

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Preventive Measures:

USE EFFECTIVE FUME REMOVAL DEVICE /IN LABORATORY/.
[Association of Official Analytical Chemists. Official Methods of Analysis. 10th ed. and supplements. Washington, DC: Association of Official Analytical Chemists, 1965. New editions through13th ed. plus supplements, 1982.,p. 13/882 51.057]**PEER REVIEWED**

Employees should wash promptly when skin is wet or contaminated. Remove clothing immediately if wet or contaminated to avoid flammability hazard.
[Sittig, M. Handbook of Toxic and Hazardous Chemicals and Carcinogens, 1985. 2nd ed. Park Ridge, NJ: Noyes Data Corporation, 1985. 409]**PEER REVIEWED**

Avoid breathing vapors. Keep upwind. Wear appropriate chemical protective gloves, boots and goggles. Do not handle broken packages unless wearing appropriate personal protective equipment. Wash away any material which may have contacted the body with copious amounts of water or soap and water.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 439]**PEER REVIEWED**

Contact lenses should not be worn when working with this chemical.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 131]**QC REVIEWED**

SRP: The scientific literature for the use of contact lenses in industry is conflicting. The benefit or detrimental effects of wearing contact lenses depend not only upon the substance, but also on factors including the form of the substance, characteristics and duration of the exposure, the uses of other eye protection equipment, and the hygiene of the lenses. However, there may be individual substances whose irritating or corrosive properties are such that the wearing of contact lenses would be harmful to the eye. In those specific cases, contact lenses should not be worn. In any event, the usual eye protection equipment should be worn even when contact lenses are in place.
PEER REVIEWED

If material not on fire and not involved in fire: Keep sparks, flames and other sources of ignition away. Keep material out of water sources and sewers. Build dikes to contain flow as necessary. Attempt to stop leak if without undue personnel hazard. Use water spray to disperse vapors and dilute standing pools of liquid.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 439]**PEER REVIEWED**

SRP: Contaminated protective clothing should be segregated in such a manner so that there is no direct

personal contact by personnel who handle, dispose, or clean the clothing. Quality assurance to ascertain the completeness of the cleaning procedures should be implemented before the decontaminated protective clothing is returned for reuse by the workers. Contaminated clothing should not be taken home at end of shift, but should remain at employee's place of work for cleaning.
PEER REVIEWED

The worker should immediately wash the skin when it becomes contaminated.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 131]**QC REVIEWED**

Work clothing that becomes wet should be immediately removed due to its flammability hazard.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 131]**QC REVIEWED**

An analysis of breakthrough times of low boiling organic solvent vapors in a commercial respirator cartridge under steady state and pulsating flow conditions was performed. A KGC-8 respirator cartridge packed with 22.5 grams of activated charcoal was exposed to 0, 100, 300, or 900 ppm carbon-tetrachloride, **ethyl-acetate,** methyl-acetate, acetone, or dichloromethane vapor under steady state or pulsed flow conditions in custom built apparatus. The steady state flow condition was achieved by setting the respirator cartridge in its holder and passing each solvent vapor through it at a flow rate of 30 liter per minute (l/min). The pulsating flow condition was achieved placing the respirator cartridge in a Tedler bag, expanding the bag by introducing each test vapor, and 'inhaling' the test vapor through the respirator cartridge using a breathing machine drawing 1.5 liters air per cycle at the rate 20 cycles/min. The total flow rate was adjusted to be similar to the 301/min rate utilized the steady state flow experiments. Solvent vapor concentrations were measured upstream and downstream from the cartridge by gas chromatography. Breakthrough times were determined as the time required for the solvent vapor concentrations downstream from the cartridge to increase to 5 ppm. The data were analyzed by logistic regression techniques. After converting the data to logarithms, the breakthrough times of all five solvents were linearly, inversely proportional to their initial concentrations under both steady state and pulsed flow conditions. The slopes of the lines were smaller for the solvents with the lower boiling points. The ratios of the breakthrough times measured under the pulsating flow to the steady slate flow condition (B/A ratio) varied from 0.77 to 0.71 for dichloromethane. The B/A ratios for the lOO ppm initial concentrations of the other four solvents varied only from 0.95 to 1.01. This indicated that except in the case of dichloromethane, there are no large differences in breakthrough tire under the two different flow conditions at lOO ppm. At the other concentrations, in each experiment as the concentration of the test vapor increased the breakthrough times under the pulsating flow condition became shorter compared to the steady state flow condition. /It was/ concluded that breakthrough of low boiling solvent vapors in respirator cartridges occurs earlier under pulsating flow than under steady state conditions.
[Tanaka S et al; Industrial Health 34 (2): 125-31 (1996)]**PEER REVIEWED**

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Stability/Shelf Life:

SLOWLY DECOMP BY MOISTURE.

[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 3806]**PEER REVIEWED**

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Shipment Methods and Regulations:

No person may /transport,/ offer or accept a hazardous material for transportation in commerce unless that person is registered in conformance ... and the hazardous material is properly classed, described, packaged, marked, labeled, and in condition for shipment as required or authorized by ... /the hazardous materials regulations (49 CFR 171-177)./
[49 CFR 171.2 (7/1/96)]**PEER REVIEWED**

The International Air Transport Association (IATA) Dangerous Goods Regulations are published by the IATA Dangerous Goods Board pursuant to IATA Resolutions 618 and 619 and constitute a manual of industry carrier regulations to be followed by all IATA Member airlines when transporting hazardous materials.
[IATA. Dangerous Goods Regulations. 38th ed. Montreal, Canada and Geneva, Switzerland: International Air Transport Association, Dangerous Goods Board, January, 1997. 146]**PEER REVIEWED**

The International Maritime Dangerous Goods Code lays down basic principles for transporting hazardous chemicals. Detailed recommendations for individual substances and a number of recommendations for good practice are included in the classes dealing with such substances. A general index of technical names has also been compiled. This index should always be consulted when attempting to locate the appropriate procedures to be used when shipping any substance or article.
[IMDG; International Maritime Dangerous Goods Code; International Maritime Organization p.3075 (1988)]**PEER REVIEWED**

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Storage Conditions:

KEEP TIGHTLY CLOSED IN COOL PLACE & AWAY FROM FIRE.
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 3806]**PEER REVIEWED**

DURING TRANSPORT: STABLE DURING TRANSPORT. STORAGE TEMPERATURE: AMBIENT. VENTING: OPEN (FLAME ARRESTER) OR PRESSURE-VACUUM.
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

On storage, it is slowly decomposed by water.
[Snyder, R. (ed.). Ethel Browning's Toxicity and Metabolism of Industrial Solvents. Second Edition. Volume 3 Alcohols and Esters. New York, NY: Elsevier, 1992. 234]**PEER REVIEWED**

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Cleanup Methods:

1. REMOVE ALL IGNITION SOURCES. 2. VENTILATE AREA OF SPILL OR LEAK. 3. FOR SMALL QUANTITIES, ABSORB ON PAPER TOWELS. EVAPORATE IN A SAFE PLACE (SUCH AS A FUME HOOD). ALLOW SUFFICIENT TIME FOR EVAPORATING VAPORS TO COMPLETELY CLEAR THE HOOD DUCTWORK. BURN THE PAPER IN A SUITABLE LOCATION AWAY FROM COMBUSTIBLE MATERIALS. LARGE QUANTITIES CAN BE COLLECTED AND ATOMIZED IN A SUITABLE COMBUSTION CHAMBER. **ETHYL ACETATE** SHOULD NOT BE ALLOWED TO ENTER A CONFINED SPACE, SUCH AS A SEWER, BECAUSE OF THE POSSIBILITY OF AN EXPLOSION.
[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) PublicationNo. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981. 3]**PEER REVIEWED**

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Disposal Methods:

Generators of waste (equal to or greater than 100 kg/mo) containing this contaminant, EPA hazardous waste numbers U112 and F003, must conform with USEPA regulations in storage, transportation, treatment and disposal of waste.
[40 CFR 240-280, 300-306, 702-799 (7/1/89)]**PEER REVIEWED**

Incineration: Burn waste material in an approved waste disposal incinerator.
[United Nations. Treatment and Disposal Methods for Waste Chemicals (IRPTC File). Data Profile Series No. 5. Geneva, Switzerland: United Nations Environmental Programme, Dec. 1985. 72]**PEER REVIEWED**

1. BY ABSORBING IT IN VERMICULITE, DRY SAND, EARTH, OR A SIMILAR MATERIAL. 2. BY ATOMIZING IN A SUITABLE COMBUSTION CHAMBER.
[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) PublicationNo. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981. 3]**PEER REVIEWED**

Ethyl acetate is a waste chemical stream constituent which may be subjected to ultimate disposal by controlled incineration.
[USEPA; Engineering Handbook for Hazardous Waste Incineration p.2-6 (1981) EPA 68-03-3025]**PEER REVIEWED**

A good candidate for rotary kiln incineration at a temperature range of 820 to 1,600 deg C and residence times of seconds for liquids and gases, and hours for solids. A good candidate for liquid injection incineration at a temperature range of 650 to 1,600 deg C and a residence time of 0.1 to 2 seconds. A good candidate for fluidized bed incineration at a temperature range of 450 to 980 deg C and residence times of seconds for liquids and gases, and longer for solids.
[USEPA; Engineering Handbook for Hazardous Waste Incineration p.3-13 (1981) EPA 68-03-3025]**PEER REVIEWED**

The following wastewater treatment technologies have been investigated for **Ethyl acetate:**
Concentration process: Biological treatment.
[USEPA; Management of Hazardous Waste Leachate, EPA Contract No.68-03-2766 p.E-33 (1982)]**PEER REVIEWED**

The following wastewater treatment technologies have been investigated for **Ethyl acetate:**
Concentration process: Activated carbon.
[USEPA; Management of Hazardous Waste Leachate, EPA Contract No.68-03-2766 p.E-133 (1982)]**PEER REVIEWED**

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Occupational Exposure Standards:

OSHA Standards:

Permissible Exposure Limit: Table Z-1 8-hr Time Weighted Avg: 400 ppm (1400 mg/cu m).
[29 CFR 1910.1000 (7/1/98)]**QC REVIEWED**

Threshold Limit Values:

8 hr Time Weighted Avg (TWA) 400 ppm
[American Conference of Governmental Industrial Hygienists. Threshold Limit Values (TLVs) for Chemical Substances and Physical Agents Biological Exposure Indices for 1998. Cincinnati, OH: ACGIH, 1998. 36]**QC REVIEWED**

Excursion Limit Recommendation: Excursions in worker exposure levels may exceed three times the TLV-TWA for no more than a total of 30 min during a work day, and under no circumstances should they exceed five times the TLV-TWA, provided that the TLV-TWA is not exceeded.
[American Conference of Governmental Industrial Hygienists. Threshold Limit Values (TLVs) for Chemical Substances and Physical Agents Biological Exposure Indices for 1998. Cincinnati, OH: ACGIH, 1998. 6]**QC REVIEWED**

NIOSH Recommendations:

Recommended Exposure Limit: 10 Hr Time-Weighted Avg: 400 ppm (1400 mg/cu m).
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 130]**QC REVIEWED**

Immediately Dangerous to Life or Health:

2000 ppm (Based on 10% of the lower explosive limit for safety considerations even though the relevant toxicological data indicated that irreversible health effects or impairment of escape existed only at higher concentrations.)
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 130]**QC REVIEWED**

Other Occupational Permissible Levels:

USSR (1973): 55 ppm; Czechoslovakia (1969): 110 ppm; Sweden (1974): 300 ppm; Italy (1975): 220 ppm.
[American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure

Indices. 5th ed. Cincinnati, OH:American Conference of Governmental Industrial Hygienists, 1986.]**PEER REVIEWED**

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[American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices. 5th ed. Cincinnati, OH:American Conference of Governmental Industrial Hygienists, 1986.]**PEER REVIEWED**

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Manufacturing/Use Information:

Major Uses:

The active ingredient is no longer contained in any registered pesticide products ... "cancelled."
[USEPA/OPP; Status of Pesticides in Registration, Reregistration and Special Review p.292 (Spring, 1998) EPA 738-R-98-002]**QC REVIEWED**

ARTIFICIAL FRUIT ESSENCES; SOLVENT FOR NITROCELLULOSE, VARNISHES, LACQUERS, AEROPLANE DOPES; MANUFACTURE OF SMOKELESS POWDER, ARTIFICIAL LEATHER, & PHOTOGRAPHIC FILMS & PLATES, ARTIFICIAL SILK, PERFUMES; CLEANING TEXTILES; PHARMACEUTIC AID (FLAVOR)
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 641]**PEER REVIEWED**

SYNTHETIC FLAVORING; USED IN FOODS
[Fenaroli's Handbook of Flavor Ingredients. Volume 2. Edited, translated, and revised by T.E. Furia and N. Bellanca. 2nd ed. Cleveland: The Chemical Rubber Co., 1975. 157]**PEER REVIEWED**

FOR CONTACT LENS MOLD RELEASE.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 2977]**PEER REVIEWED**

SOLVENT FOR COATINGS (EG, SHELLAC) & PLASTICS (EG, VINYL RESINS); OTHER SOLVENT USES (EG, INKS); CHEM INTERMEDIATE; AROMA ENHANCER IN GRAPE BEVERAGES.
[SRI]**PEER REVIEWED**

Organic synthesis
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 12th ed. New York, NY: Van Nostrand Rheinhold Co., 1993 478]**PEER REVIEWED**

Solvent in production of adhesives, fingernail polishes; extraction solvent in production of pharmaceuticals and foods; carrier solvent for herbicides; component of lacquer thinner.
[CHEMICAL PRODUCTS SYNOPSIS: Ethyl Acetate (1983)]**PEER REVIEWED**

MEDICATION
PEER REVIEWED

/Used/ ... as diluents in inks for marking fruits and vegetables.
[21 CFR 73.1 (4/1/97)]**PEER REVIEWED**

In the manufacture of vaccines, splitting influenza virus.
[Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984.,p. V23 632 (83)]**PEER REVIEWED**

In fruit and brandy flavors.
[Gerhartz, W. (exec ed.). Ullmann's Encyclopedia of Industrial Chemistry. 5th ed.Vol A1: Deerfield Beach, FL: VCH Publishers, 1985 to Present.,p. VA11 152]**PEER REVIEWED**

Manufacturers:

Eastman Chemical Company, Hq, P.O. Box 511, Kingsport, TN 37662, (423) 229-2000; Tennessee Eastman Division, Hq, P.O Box 511, Kingsport, TN 37662, (423) 229-2000; Production site: Kingsport, TN 37662; Texas Eastman Division, Hq, P.O. Box 744, Longview, TX 75607-7444, (903) 237-5000; Production site: Longview, TX 75607
[SRI. 1997 Directory of Chemical Producers - United States of America. Menlo Park, CA: SRI International 1997. 583]**PEER REVIEWED**

Hoechst Celanese Corp, Hq, Route 202-206 North, P.O. Box 2500, Somerville, NJ 08876, (908) 231-2000; Celanese Ltd., Hq, 1601 West LBJ Freeway, Dallas, TX 75381, (972) 277-4000; Chemicals Division; Production site: P.O. Box 937, Pampa, TX 79065
[SRI. 1997 Directory of Chemical Producers - United States of America. Menlo Park, CA: SRI International 1997. 583]**PEER REVIEWED**

Monsanto Company, Hq, 800 North Lindbergh Boulevard, St. Louis, MO 63167, (314) 694-1000; Chemical Group; Production sites: 730 Worcester Street, Springfield, MA 01151 (Indian Orchard Plant); 5100 W. Jefferson, Trenton, MI 48183
[SRI. 1997 Directory of Chemical Producers - United States of America. Menlo Park, CA: SRI International 1997. 583]**PEER REVIEWED**

Methods of Manufacturing:

Co-product of butane oxidation to acetic acid at 175 deg C and 50 atm in the presence of catalytic cobalt and chromium ions; co-product of the ethanolysis of polyvinyl acetate to polyvinyl alcohol.
[CHEMICAL PRODUCTS SYNOPSIS: Ethyl Acetate (1983)]**PEER REVIEWED**

Acetaldehyde (Tishchenko reaction); ethanol + acetic acid (esterification); polyvinyl acetate + ethanol (transesterification; byproduct of polyvinyl alcohol reaction).
[Ashford, R.D. Ashford's Dictionary of Industrial Chemicals. London, England: Wavelength Publications Ltd., 1994. 387]**PEER REVIEWED**

By heating acetic acid and ethyl alcohol in presence of sulfuric acid and distilling.
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 12th ed. New York, NY: Van Nostrand Rheinhold Co., 1993 477]**PEER REVIEWED**

Formulations/Preparations:

GRADES: COMMERCIAL, 85-88%; 95-98%; 99%; NF /NATIONAL FORMULARY GRADE OF CHEMICAL/ (99%); FCC /FOOD CHEMICAL CODEX/.
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 12th ed. New York, NY: Van Nostrand Rheinhold Co., 1993 478]**PEER REVIEWED**

Nail polish remover typically 40 wt% **ethyl acetate.**
[Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984.,p. V7 163]**PEER REVIEWED**

Impurities:

In the 85-88% grade, the major constituent other than **ethyl acetate** is ethanol.
[CHEMICAL PRODUCTS SYNOPSIS: Ethyl Acetate (1983)]**PEER REVIEWED**

Consumption Patterns:

SOLVENT FOR: COATINGS (EG, SHELLAC), 65%; PLASTICS (EG, VINYL RESINS), 12%; OTHER SOLVENT USES (EG, INKS), 20%; CHEM INTERMEDIATE, 3% (1983)
[SRI]**PEER REVIEWED**

Lacquers and enamels, 60%; inks, 15%; miscellaneous, 25% (1983) /estimate/
[CHEMICAL PRODUCTS SYNOPSIS: Ethyl Acetate (1983)]**PEER REVIEWED**

CHEMICAL PROFILE: **Ethyl Acetate.** Coatings solvent, 40%; exports, 38%; miscellaneous solvent uses, 12%; plastics, 8%; chemical synthesis, 2%.
[Kavaler AR; Chemical Marketing Reporter 235 (2): 46 (1989)]**PEER REVIEWED**

CHEMICAL PROFILE: **Ethyl acetate.** Demand: 1988: 210 million lb; 1989: 210 million lb; 1993 /projected/: 220 million lb. (Includes exports, but not imports, which totaled 30 million lb last year.)
[Kavaler AR; Chemical Marketing Reporter 235 (2): 46 (1989)]**PEER REVIEWED**

CHEMICAL PROFILE: **Ethyl Acetate.** Demand, million pounds: 325 in 1996, 335 in 1997, est 400 in 2001 (includes exports of 100 to 125 million pounds; but not imports in the range of 20 million to 30 million pounds annually). Uses: coatings solvent, 60%; process solvent, including pharmaceuticals and organic synthesis, 15%; inks solvent, 15%; miscellaneous solvent uses, including adhesives and cosmetics, 10%.
[Kavaler AR; Chemical Marketing Reporter, Oct 6, 1997 (1997)]**PEER REVIEWED**

U. S. Production:

(1978) 8.26X10+10 G
[SRI]**PEER REVIEWED**

(1982) 1.07X10+11 G
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(1985) 8.71X10+10 g
[USITC. SYN ORG CHEM-U.S. PROD/SALES p.266 (1985)]**PEER REVIEWED**

(1986) 1.92X10+8 lb
[USITC. SYN ORG CHEM-U.S. PROD/SALES. PRELIMINARY p.C/P-87-5 (1986)]**PEER REVIEWED**

U. S. Imports:

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[SRI]**PEER REVIEWED**

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[SRI]**PEER REVIEWED**

(1985) 4.40X10+9 g
[BUREAU OF THE CENSUS. U.S. IMPORTS FOR CONSUMPTION AND GENERAL IMPORTS p.1-582 (1985)]**PEER REVIEWED**

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ETHYL ACETATE

CASRN: 141-78-6

For other data, click on the Table of Contents

Major Uses:

The active ingredient is no longer contained in any registered pesticide products ... "cancelled."
[USEPA/OPP; Status of Pesticides in Registration, Reregistration and Special Review p.292 (Spring, 1998) EPA 738-R-98-002]**QC REVIEWED**

ARTIFICIAL FRUIT ESSENCES; SOLVENT FOR NITROCELLULOSE, VARNISHES, LACQUERS, AEROPLANE DOPES; MANUFACTURE OF SMOKELESS POWDER, ARTIFICIAL LEATHER, & PHOTOGRAPHIC FILMS & PLATES, ARTIFICIAL SILK, PERFUMES; CLEANING TEXTILES; PHARMACEUTIC AID (FLAVOR)
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 641]**PEER REVIEWED**

SYNTHETIC FLAVORING; USED IN FOODS
[Fenaroli's Handbook of Flavor Ingredients. Volume 2. Edited, translated, and revised by T.E. Furia and N. Bellanca. 2nd ed. Cleveland: The Chemical Rubber Co., 1975. 157]**PEER REVIEWED**

FOR CONTACT LENS MOLD RELEASE.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 2977]**PEER REVIEWED**

SOLVENT FOR COATINGS (EG, SHELLAC) & PLASTICS (EG, VINYL RESINS); OTHER SOLVENT USES (EG, INKS); CHEM INTERMEDIATE; AROMA ENHANCER IN GRAPE BEVERAGES.
[SRI]**PEER REVIEWED**

Organic synthesis
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 12th ed. New York, NY: Van Nostrand Rheinhold Co., 1993 478]**PEER REVIEWED**

Solvent in production of adhesives, fingernail polishes; extraction solvent in production of pharmaceuticals and foods; carrier solvent for herbicides; component of lacquer thinner.
[CHEMICAL PRODUCTS SYNOPSIS: Ethyl Acetate (1983)]**PEER REVIEWED**

MEDICATION
PEER REVIEWED

/Used/ ... as diluents in inks for marking fruits and vegetables.
[21 CFR 73.1 (4/1/97)]**PEER REVIEWED**

In the manufacture of vaccines, splitting influenza virus.

[Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984.,p. V23 632 (83)]**PEER REVIEWED**

In fruit and brandy flavors.
[Gerhartz, W. (exec ed.). Ullmann's Encyclopedia of Industrial Chemistry. 5th ed.Vol A1: Deerfield Beach, FL: VCH Publishers, 1985 to Present.,p. VA11 152]**PEER REVIEWED**

ETHYL ACETATE

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For other data, click on the Table of Contents

Manufacturers:

Eastman Chemical Company, Hq, P.O. Box 511, Kingsport, TN 37662, (423) 229-2000; Tennessee Eastman Division, Hq, P.O Box 511, Kingsport, TN 37662, (423) 229-2000; Production site: Kingsport, TN 37662; Texas Eastman Division, Hq, P.O. Box 744, Longview, TX 75607-7444, (903) 237-5000; Production site: Longview, TX 75607

[SRI. 1997 Directory of Chemical Producers - United States of America. Menlo Park, CA: SRI International 1997. 583]**PEER REVIEWED**

Hoechst Celanese Corp, Hq, Route 202-206 North, P.O. Box 2500, Somerville, NJ 08876, (908) 231-2000; Celanese Ltd., Hq, 1601 West LBJ Freeway, Dallas, TX 75381, (972) 277-4000; Chemicals Division; Production site: P.O. Box 937, Pampa, TX 79065

[SRI. 1997 Directory of Chemical Producers - United States of America. Menlo Park, CA: SRI International 1997. 583]**PEER REVIEWED**

Monsanto Company, Hq, 800 North Lindbergh Boulevard, St. Louis, MO 63167, (314) 694-1000; Chemical Group; Production sites: 730 Worcester Street, Springfield, MA 01151 (Indian Orchard Plant); 5100 W. Jefferson, Trenton, MI 48183

[SRI. 1997 Directory of Chemical Producers - United States of America. Menlo Park, CA: SRI International 1997. 583]**PEER REVIEWED**

ETHYL ACETATE

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[BUREAU OF THE CENSUS. U. S. EXPORTS, SCHEDULE E, P.2-59 (JANUARY 1988)]**PEER REVIEWED**

ETHYL ACETATE

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For other data, click on the Table of Contents

Laboratory Methods:

Clinical Laboratory Methods:

WHEN GAS CHROMATOGRAPHIC-MASS SPECTROSCOPY WAS USED IN ANALYSIS, **ETHYL ACETATE** WAS DETECTED IN ALL BLOOD SAMPLES & BRAIN TISSUES. THE CURVES OF BLOOD ETHYL ALCOHOL CONCN VS BLOOD PH VALUES SHOWED A REGRESSION DISTRIBUTION PATTERN. THESE RESULTS MAY BE USED IN FORENSIC INVESTIGATIONS.
[KOJIMA T ET AL; NIPPON HOIGAKU ZASSHI 34 (5): 587-95 (1980)]**PEER REVIEWED**

DETECTION & IDENTIFICATION OF VOLATILE ORGANIC COMPOUNDS, INCLUDING **ETHYL ACETATE,** IN WHOLE BLOOD, PLASMA, OR SERUM BY HEADSPACE GAS CHROMATOGRAPHY AS AN AID TO THE DIAGNOSIS OF SOLVENT ABUSE.
[RAMSEY JD, FLANAGAN RJ; J CHROMATOGR 240 (2): 423-44 (1982)]**PEER REVIEWED**

Analytic Laboratory Methods:

ANALYTE: **ETHYL ACETATE.** MATRIX: AIR. PROCEDURE: ADSORPTION ON CHARCOAL, DESORPTION WITH CARBON DISULFIDE, GAS CHROMATOGRAPHY. RANGE: 704-2950 MG/CU M.
[U.S. Department of Health, Education Welfare, Public Health Service. Center for Disease Control, National Institute for Occupational Safety Health. NIOSH Manual ofAnalytical Methods. 2nd ed. Volumes 1-7. Washington, DC: U.S. Government Printing Office, 1977-present.,p. V2 S49]**PEER REVIEWED**

Residual solvents in pharmaceutical powders were determined by gas chromatography with a headspace injection system. The chromatography conditions and parameters of the injection system were optimized to enable the quantification by external standardization of 21 most common solvents in concn ranging from a few ppm to a few percent. Porapak Q (100-120 mesh) was used as the stationary phase with flame ionization detection.
[Guimbard JP et al; J chromatogr 403: 109-21 (1987)]**PEER REVIEWED**

A generalized GC method is described for the determinations of a wide variety of residual solvents and other volatile impurities in bulk pharmaceuticals. ... Analytical data from replicated determinations of 7 representative cmpd are reported.
[Haky JE, Stickney TM; J Chromatogr 321 (1): 137-44 (1985)]**PEER REVIEWED**

The head space method for determining volatile gases was developed and compared with results obtained by the conventional purge and trap method. A gas chromatogram fitted with a retractable retrofit on

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[Takeoka G, Jennings W; J Chromatrogr Sci 22 (5): 177-84 (1984)]**PEER REVIEWED**

Esters in distilled liquors, spectrophotometric method. Esters including **ethyl acetate** react quantitatively with hydroxylamine in alkaline solutions to form a hydroxamic acid which, forms colored complex with ferric ions. Ester concentration is proportional to absorbance at 525 nm at constant alcohol concentration and is calculated from standard curves.
[Association of Official Analytic Chemists. Official Methods of Analysis of the AOAC. 14th ed. Arlington, VA: Association of Official Analytic Chemists, Inc., 1984. 182]**PEER REVIEWED**

NIOSH Method 1457. Determination of **Ethyl Acetate** by Gas Chromatography with Flame Ionization Detection, GC/FID, workplace air, detection limit, 0.050 mg/cu m.
[U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSH Manual of Analytical Methods. 4th ed.Methods A-Z & Supplements. Washington, DC: U.S. Government Printing Office, Aug 1994.]**PEER REVIEWED**

AOAC Method 972.10. Alcohols (Higher) and **Ethyl Acetate** in Distilled Liquors. Alternative Gas Chromatographic Method.
[Association of Official Analytical Chemists. Official Methods of Analysis. 15th ed. and Supplements. Washington, DC: Association of Analytical Chemists, 1990 700]**PEER REVIEWED**

AOAC Method 968.09. Alcohols (Higher) and **Ethyl Acetate** in Distilled Liquors. Gas Chromatographic Method.
[Association of Official Analytical Chemists. Official Methods of Analysis. 15th ed. and Supplements. Washington, DC: Association of Analytical Chemists, 1990 700]**PEER REVIEWED**

Sampling Procedures:

ETHYL ACETATE VAPORS ARE ADSORBED ONTO SILICA GEL CONTAINED IN A LIGHTWEIGHT ALUMINUM ALLOY SAMPLING TUBE FOR USE IN DESORPTION AND ANALYTICAL TECHNIQUES.
[LEE GL, WALDRON T; ANN OCCUP HYG 19 (2): 129 (1976)]**PEER REVIEWED**

The field data of solvent concentrations were determined using active and passive samplers, and compared to values obtained from urinary analyses. Active samplers were taken by activated charcoal tubes; passive samples were taken by the TK200 passive dosimeters. /It was concluded/ that passive dosimeters are reliable and represent a viable alternative for determination of solvents in air.
[Bartolucci GB; Ann Occup Hyg 30 (3): 295-306 (1986)]**PEER REVIEWED**

Analyte: **Ethyl acetate;** Matrix: Air; Procedure: Adsorption on charcoal. Sample size: 6 liters; Precision

for total analytical and sampling method in the range of 704-2950 mg/cu m was 0.058, Flow rate: + or - 5 percent.
[U.S. Department of Health, Education Welfare, Public Health Service. Center for Disease Control, National Institute for Occupational Safety Health. NIOSH Manual ofAnalytical Methods. 2nd ed. Volumes 1-7. Washington, DC: U.S. Government Printing Office, 1977-present.,p. S49-1]**PEER REVIEWED**

ETHYL ACETATE

CASRN: 141-78-6

For other data, click on the Table of Contents

Clinical Laboratory Methods:

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ETHYL ACETATE

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Synonyms and Identifiers:

Synonyms:

ACETATE D'ETHYLE (FRENCH)
PEER REVIEWED

Acetato de etilo (Spanish)
PEER REVIEWED

ACETIC ACID, ETHYL ESTER
PEER REVIEWED

ACETIC ETHER
PEER REVIEWED

Acetidin
PEER REVIEWED

Acetoxyethane
PEER REVIEWED

Aethylacetat (German)
PEER REVIEWED

AI3-00404
PEER REVIEWED

Caswell No 429
PEER REVIEWED

EPA Pesticide Chemical Code 044003
PEER REVIEWED

ESSIGESTER (GERMAN)
PEER REVIEWED

ETHYLACETAAT (DUTCH)
PEER REVIEWED

ETHYL ACETIC ESTER
PEER REVIEWED

ETHYLE (ACETATE D') (FRENCH)
PEER REVIEWED

ETHYL ESTER

PEER REVIEWED

ETHYLESTER KYSELINY OCTOVE (CZECH)
PEER REVIEWED

ETHYL ETHANOATE
PEER REVIEWED

ETILE (ACETATO DI) (ITALIAN)
PEER REVIEWED

OCTAN ETYLU (POLISH)
PEER REVIEWED

VINEGAR NAPHTHA
PEER REVIEWED

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Shipping Name/ Number DOT/UN/NA/IMO:

UN 1173; **Ethyl acetate**

IMO 3.2; **Ethyl acetate**

Standard Transportation Number:

49 091 60; **Ethyl acetate**

EPA Hazardous Waste Number:

U112; A toxic waste when a discarded commercial chemical product or manufacturing chemical intermediate or an off-specification commercial chemical product.

F003; A hazardous waste from nonspecific sources when a spent solvent.

RTECS Number:

NIOSH/AH5425000

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PEER REVIEWED

Acetato de etilo (Spanish)
PEER REVIEWED

ACETIC ACID, ETHYL ESTER
PEER REVIEWED

ACETIC ETHER
PEER REVIEWED

Acetidin
PEER REVIEWED

Acetoxyethane
PEER REVIEWED

Aethylacetat (German)
PEER REVIEWED

AI3-00404
PEER REVIEWED

Caswell No 429
PEER REVIEWED

EPA Pesticide Chemical Code 044003
PEER REVIEWED

ESSIGESTER (GERMAN)
PEER REVIEWED

ETHYLACETAAT (DUTCH)
PEER REVIEWED

ETHYL ACETIC ESTER
PEER REVIEWED

ETHYLE (ACETATE D') (FRENCH)
PEER REVIEWED

ETHYL ESTER
PEER REVIEWED

ETHYLESTER KYSELINY OCTOVE (CZECH)

PEER REVIEWED

ETHYL ETHANOATE
PEER REVIEWED

ETILE (ACETATO DI) (ITALIAN)
PEER REVIEWED

OCTAN ETYLU (POLISH)
PEER REVIEWED

VINEGAR NAPHTHA
PEER REVIEWED

ETHYL ACETATE

CASRN: 141-78-6

For other data, click on the Table of Contents

Shipping Name/ Number DOT/UN/NA/IMO:

UN 1173; **Ethyl acetate**

IMO 3.2; **Ethyl acetate**

ETHYL ACETATE

CASRN: 141-78-6

For other data, click on the Table of Contents

Standard Transportation Number:

49 091 60; **Ethyl acetate**

ETHYL ACETATE

CASRN: 141-78-6

For other data, click on the Table of Contents

EPA Hazardous Waste Number:

U112; A toxic waste when a discarded commercial chemical product or manufacturing chemical intermediate or an off-specification commercial chemical product.

F003; A hazardous waste from nonspecific sources when a spent solvent.

ETHYL ACETATE

CASRN: 141-78-6

For other data, click on the Table of Contents

RTECS Number:

NIOSH/AH5425000

ETHYL ACETATE

CASRN: 141-78-6

For other data, click on the Table of Contents

Administrative Information:

Hazardous Substances Databank Number: 83

Last Revision Date: 20000313

Last Review Date: Reviewed by SRP on 5/7/1998

Update History:

Complete Update on 03/13/2000, 2 fields added/edited/deleted.
Complete Update on 01/11/2000, 6 fields added/edited/deleted.
Field Update on 08/26/1999, 1 field added/edited/deleted.
Complete Update on 06/03/1999, 1 field added/edited/deleted.
Complete Update on 01/20/1999, 1 field added/edited/deleted.
Complete Update on 11/12/1998, 1 field added/edited/deleted.
Complete Update on 07/27/1998, 74 fields added/edited/deleted.
Complete Update on 03/27/1997, 2 fields added/edited/deleted.
Complete Update on 03/11/1997, 2 fields added/edited/deleted.
Complete Update on 02/24/1997, 1 field added/edited/deleted.
Complete Update on 12/11/1996, 1 field added/edited/deleted.
Complete Update on 06/27/1996, 1 field added/edited/deleted.
Complete Update on 05/14/1996, 1 field added/edited/deleted.
Complete Update on 05/10/1996, 1 field added/edited/deleted.
Complete Update on 04/16/1996, 8 fields added/edited/deleted.
Field Update on 01/18/1996, 1 field added/edited/deleted.
Complete Update on 01/20/1995, 1 field added/edited/deleted.
Complete Update on 12/19/1994, 1 field added/edited/deleted.
Complete Update on 11/18/1994, 1 field added/edited/deleted.
Complete Update on 07/25/1994, 1 field added/edited/deleted.
Complete Update on 03/25/1994, 1 field added/edited/deleted.
Complete Update on 08/24/1993, 1 field added/edited/deleted.
Complete Update on 08/10/1993, 2 fields added/edited/deleted.
Complete Update on 08/07/1993, 1 field added/edited/deleted.
Complete Update on 08/04/1993, 1 field added/edited/deleted.
Field update on 12/10/1992, 1 field added/edited/deleted.
Complete Update on 11/20/1992, 1 field added/edited/deleted.
Complete Update on 04/27/1992, 1 field added/edited/deleted.
Complete Update on 01/23/1992, 1 field added/edited/deleted.
Complete Update on 05/31/1991, 1 field added/edited/deleted.
Complete Update on 05/08/1991, 51 fields added/edited/deleted.
Complete Update on 06/29/1990, 10 fields added/edited/deleted.
Complete Update on 05/21/1990, 3 fields added/edited/deleted.

Complete Update on 04/16/1990, 3 fields added/edited/deleted.
Complete Update on 01/11/1990, 2 fields added/edited/deleted.
Field update on 12/29/1989, 1 field added/edited/deleted.
Complete Update on 08/17/1989, 91 fields added/edited/deleted.
Complete Update on 10/03/1986

Record Length: 143454

ETHYL ACETATE

CASRN: 141-78-6

For other data, click on the Table of Contents

Hazardous Substances Databank Number: 83

ETHYL ACETATE

CASRN: 141-78-6

For other data, click on the Table of Contents

Last Revision Date: 20000313

ETHYL ACETATE

CASRN: 141-78-6

For other data, click on the Table of Contents

Last Review Date: Reviewed by SRP on 5/7/1998

ETHYL ACETATE

CASRN: 141-78-6

For other data, click on the Table of Contents

Update History:

Complete Update on 03/13/2000, 2 fields added/edited/deleted.
Complete Update on 01/11/2000, 6 fields added/edited/deleted.
Field Update on 08/26/1999, 1 field added/edited/deleted.
Complete Update on 06/03/1999, 1 field added/edited/deleted.
Complete Update on 01/20/1999, 1 field added/edited/deleted.
Complete Update on 11/12/1998, 1 field added/edited/deleted.
Complete Update on 07/27/1998, 74 fields added/edited/deleted.
Complete Update on 03/27/1997, 2 fields added/edited/deleted.
Complete Update on 03/11/1997, 2 fields added/edited/deleted.
Complete Update on 02/24/1997, 1 field added/edited/deleted.
Complete Update on 12/11/1996, 1 field added/edited/deleted.
Complete Update on 06/27/1996, 1 field added/edited/deleted.
Complete Update on 05/14/1996, 1 field added/edited/deleted.
Complete Update on 05/10/1996, 1 field added/edited/deleted.
Complete Update on 04/16/1996, 8 fields added/edited/deleted.
Field Update on 01/18/1996, 1 field added/edited/deleted.
Complete Update on 01/20/1995, 1 field added/edited/deleted.
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Complete Update on 11/18/1994, 1 field added/edited/deleted.
Complete Update on 07/25/1994, 1 field added/edited/deleted.
Complete Update on 03/25/1994, 1 field added/edited/deleted.
Complete Update on 08/24/1993, 1 field added/edited/deleted.
Complete Update on 08/10/1993, 2 fields added/edited/deleted.
Complete Update on 08/07/1993, 1 field added/edited/deleted.
Complete Update on 08/04/1993, 1 field added/edited/deleted.
Field update on 12/10/1992, 1 field added/edited/deleted.
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Complete Update on 06/29/1990, 10 fields added/edited/deleted.
Complete Update on 05/21/1990, 3 fields added/edited/deleted.
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Complete Update on 01/11/1990, 2 fields added/edited/deleted.
Field update on 12/29/1989, 1 field added/edited/deleted.
Complete Update on 08/17/1989, 91 fields added/edited/deleted.
Complete Update on 10/03/1986

ETHYL ACETATE

CASRN: 141-78-6

For other data, click on the Table of Contents

Record Length: 143454

Best Sections

1 Formulations/Preparations
2 Formulations/Preparations
3 Consumption Patterns
4 Analytic Laboratory Methods
5 Other Chemical/Physical Properties
6 Consumption Patterns
7 Other Chemical/Physical Properties

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Drug Warnings
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☐ Emergency Medical Treatment
☐ Emergency Medical Treatment
☐ Animal Toxicity Studies
☐ Non-Human Toxicity Excerpts
☐ Non-Human Toxicity Values
☐ Ecotoxicity Values
☐ Ongoing Test Status

ETHANOL

CASRN: 64-17-5

For other data, click on the Table of Contents

Best Sections

Formulations/Preparations :

To every 100 gal of ethyl alcohol add: 4.25 gal of **ethyl acetate** having an ester content of 100% by wt or the equivalent thereof not to exceed 5 gal of **ethyl acetate** with an ester content of not less than 85% by wt
[Flick, E.W. Industrial Solvents Handbook. 3rd ed. Park Ridge, NJ: Noyes Publications, 1985. 212]**PEER REVIEWED**

Formulations/Preparations :

To every 100 gal of ethyl alcohol add: 29.75 gal of **ethyl acetate** having an ester content of 100% by wt or the equivalent thereof not to exceed 35 gal of **ethyl acetate** with an ester content of not less than 85% by wt
[Flick, E.W. Industrial Solvents Handbook. 3rd ed. Park Ridge, NJ: Noyes Publications, 1985. 212]**PEER REVIEWED**

Consumption Patterns :

MOTOR FUEL SUPPLEMENT, 25%; SOLVENT FOR: TOILETRIES & COSMETICS, 11%; COATINGS, INKS & PROPRIETARY BLENDS, 11%; DETERGENTS, DISINFECTANTS & FLAVORINGS, 7%; PROCESSING, 5%; PHARMACEUTICALS, 2%; OTHER SOLVENT USES, 2%; CHEM INTERMED FOR: GLYCOL ETHERS, 6%; ETHYL ACRYLATE, 6%; ETHYL AMINES, 5%; **ETHYL ACETATE,** 3%; ACETALDEHYDE, 3%; OTHER USES, 4% (1981 NON-BEVERAGE USE)
[SRI]**PEER REVIEWED**

Analytic Laboratory Methods :

- Metabolism/Pharmacokinetics
  - Metabolism/Metabolites
  - Absorption, Distribution & Excretion
  - Mechanism of Action
  - Interactions
- Pharmacology
  - Therapeutic Uses
  - Drug Warnings
  - Interactions
  - Drug Tolerance
- Environmental Fate & Exposure
  - Environmental Fate/Exposure Summary
  - Probable Routes of Human Exposure
  - Natural Pollution Sources
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  - Environmental Fate
  - Environmental Biodegradation
  - Environmental Abiotic Degradation
  - Environmental Bioconcentration
  - Soil Adsorption/Mobility
  - Volatilization from Water/Soil
  - Environmental Water Concentrations
  - Effluent Concentrations
  - Atmospheric Concentrations
  - Food Survey Values
- Environmental Standards & Regulations

Alcohol in wines by dichromate oxidation. Sample is steam-distilled into acidified potassium dichromate soln. Oxidation of ethanol to **ethyl acetate** is completed by heating. Unreacted dichromate is determined by titration with standard ferric ammonium sulfate soln, using o-phenanthroline as indicator. Calculate % alcohol by vol ... .
[Association of Official Analytic Chemists. Official Methods of Analysis of the AOAC. 14th ed. Arlington, VA: Association of Official Analytic Chemists, Inc., 1984.,p. 220 11.008]**PEER REVIEWED**

Other Chemical/Physical Properties :

Forms ternary azeotropes with water, acetal; water, benzene; water, bromodichlormethane; water, 1-bromo-2-methylpropane; water, cis-1-bromopropane; water, trans-bromopropane; water, 1-bromopropane; water, 2-bromopropane; water, carbon disulfide; water, chloroform; water, 1-chloro-2-methylpropane; water, cyclohexene; water, 1,2-dichloroethane; water, cis-1,2-dichloroethylene; water, trans-1,2-dichloroethylene; water, dimethoxymethane; water, **ethyl acetate;** water, ethyl chloroacetate; water, trichloroethylene; water, triethylamine
[Flick, E.W. Industrial Solvents Handbook. 3rd ed. Park Ridge, NJ: Noyes Publications, 1985. 219]**PEER REVIEWED**

Consumption Patterns :

CHEMICAL PROFILE: Synthetic ethanol: chemical intermediate (for **ethyl acetate,** ethyl acrylate, glycol ethers, ethylamines and other), 30%; toiletries and cosmetics, 20%; coatings solvent, 15%; vinegar, 10%; household cleaners, 7%; detergents, 5%; pharmaceuticals, 5%; printing inks, 3%; miscellaneous, 5%. Fermentation ethanol: fuel component, 90%; beverages, 8%; industrial (chemical and solvent) uses, 2% (1988).
[Kavaler AR; Chemical Marketing Reporter 233 (4): 62 (1988)]**PEER REVIEWED**

Other Chemical/Physical Properties :

Forms binary azeotropes with tert-amyl ethyl ether, benzene, 1-bromobutane, 2-bromobutane, cis-1-bromo-1-butene, trans-1-bromo-1-butene, cis-2-bromo-2-butene, trans-2-bromo-2-butene, 2-bromo-1-butene,

- FIFRA Requirements
- Atmospheric Standards
- FDA Requirements
- Allowable Tolerances
- Chemical/Physical Properties
  - Molecular Formula
  - Molecular Weight
  - Color/Form
  - Odor
  - Taste
  - Boiling Point
  - Melting Point
  - Critical Temperature & Pressure
  - Density/Specific Gravity
  - Dissociation Constants
  - Heat of Combustion
  - Heat of Vaporization
  - Octanol/Water Partition Coefficient
  - Solubilities
  - Spectral Properties
  - Surface Tension
  - Vapor Density
  - Vapor Pressure
  - Viscosity
  - Other Chemical/Physical Properties
- Chemical Safety & Handling
  - DOT Emergency Guidelines
  - Odor Threshold
  - Fire Potential
  - NFPA Hazard Classification
  - Flammable Limits
  - Flash Point

1-bromo-3-methylbutane, 1-bromo-1-methylpropane, 2-bromo-2-methylpropane, 1-bromopropane, 2-bromopropane, 2-bromopropane, trans-1-bromopropene, cis-1-bromopropene, tert-butyl ethyl ether, carbon disulfide, carbon tetrachloride, 1-chlorobutane, 2-chlorobutane, cis-1-chloro-1-butene, trans-1-chloro-1-butene, 2-chloro-1-butene, cis-2-chloro-2-butene, chloroform, 1-chloro-3-methylbutane, 1-chloro-2-methylpropane, 1-chloropropane, 2-chloropane, trans-1-chloropropene, 3-chloropropene, 1,3-cyclohexadiene, cyclohexane, cyclohexane, cyclopentane, 1,1-dichloropropane, 2,2-dichloropropane, 2,5-dimethylhexane, diethoxymethane, **ethyl acetate,** ethyl acrylate, ethyl propionate, ethyl propyl ether, ethyl sulfide, fluorobenzene, n-heptane, n-hexane, 2-iodobutane, 1-iodo-2-methylpropane, 1-iodopropane, 2-iodopropane, 3-iodopropene, isobutyl formate, isoprene, isopropyl acetate, methyl acetate, methyl acrylate, methyl borate, 2-methylbutane, methyl butyrate, methyl carbonate, methylcyclopentene, methylcyclopentene, methyl ethyl ketone, methyl propionate, octane, pentane, 2-pentanone, perchloroethylene, propanediol, propyl acetate, propyl ether, thiophene, toluene, trichloroethylene
[Flick, E.W. Industrial Solvents Handbook. 3rd ed. Park Ridge, NJ: Noyes Publications, 1985. 219]**PEER REVIEWED**

- [ ] Autoignition Temperature
- [ ] Fire Fighting Procedures
- [ ] Explosive Limits & Potential
- [ ] Hazardous Reactivities & Incompatibilities
- [ ] Immediately Dangerous to Life or Health
- [ ] Protective Equipment & Clothing
- [ ] Preventive Measures
- [ ] Shipment Methods and Regulations
- [ ] Storage Conditions
- [ ] Cleanup Methods
- [ ] Disposal Methods
- [ ] Occupational Exposure Standards
- [ ] OSHA Standards
- [ ] Threshold Limit Values
- [ ] NIOSH Recommendations
- [ ] Immediately Dangerous to Life or Health
- [ ] Other Occupational Permissible Levels
- [ ] Manufacturing/Use Information
- [ ] Major Uses
- [ ] Manufacturers
- [ ] Methods of Manufacturing
- [ ] General Manufacturing Information
- [ ] Formulations/Preparations
- [ ] Consumption Patterns
- [ ] U. S. Production
- [ ] U. S. Imports
- [ ] U. S. Exports

- [ ] Laboratory Methods
- [ ] Clinical Laboratory Methods
- [ ] Analytic Laboratory Methods
- [ ] Sampling Procedures
- [ ] Special References
- [ ] Special Reports
- [ ] Synonyms and Identifiers
- [ ] Synonyms
- [ ] Formulations/Preparations
- [ ] Shipping Name/ Number DOT/UN/NA/IMO
- [ ] Standard Transportation Number
- [ ] RTECS Number
- [ ] Administrative Information
- [ ] Hazardous Substances Databank Number
- [ ] Last Revision Date
- [ ] Last Review Date
- [ ] Update History
- [ ] Record Length

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Metabolism/Metabolites:

The purpose of this study was to clarify whether the blood concentration of inhaled toluene, ethylbenzene, m-xylene, or mesitylene can change after the concomitant pulmonary absorption of **ethyl acetate. (**Adult female Sprague-Dawley rats were exposed in a 20 liter glass chamber under dynamic conditions for 2 hours to various concentrations of the aromatics without or in combination with different concentrations of **ethyl acetate (**0, 1000, or 4000 ppm) in air. Concentration ranges were as follows: toluene, 140-690 ppm; ethylbenzene, 120-650 ppm; m-xylene, 100-560 ppm; mesitylene, 120-720 ppm; and **ethyl acetate,** 1000 or 4000 ppm. The coexposures with **ethyl acetate** lowered the blood concentrations of other inhaled aromatics. This reduction was statistically significant following a 2 hour exposure to 230 ppm toluene in combination with 1000 ppm **ethyl acetate,** 650 ppm ethylbenzene with 1000 ppm **ethyl acetate,** and 100 ppm m-xylene with 4000 ppm **ethyl acetate.)** Similarly a significant reduction of the blood level of the aromatics by **ethyl acetate** coinhalation was also observed at higher exposure concentrations with toluene and m-xylene. A metabolic interaction such as enhanced disposition of the aromatics, may be responsible for these effects. However, it is possible that the solubility of the solvents could be altered by the presence of **ethyl acetate.** It was concluded that coexposures to concentrations in the order of the threshold limit values (100 ppm for these solvents) with 400 ppm **ethyl acetate** should not be followed by a dangerous change of the blood levels of the aromatics.

[Freundt KJ et al; Bull Environ Contam Toxicol 42 (4): 495-8 (1989)]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Human Health Effects:

Toxicity Summary:

The acute toxicity of ethylbenzene to algae, aquatic invertebrates and fish is moderate. ... No information is available regarding chronic exposure of aquatic organisms to ethylbenzene. There is limited information regarding the toxicity of ethylbenzene to bacteria ... There are no data for terrestrial plants, birds, or wild mammals. Human exposure to ethylbenzene occurs mainly by inhalation; 40-60% of inhaled ethylbenzene is retained in the lung. Ethylbenzene is extensively metabolized, mainly to mandelic and phenylglyoxylic acids. These urinary metabolites can be used to monitor human exposures. Ethylbenzene has low acute and chronic toxicity for both animals and humans. It is toxic to the central nervous system and is an irritant of mucous membranes and the eyes. ... Ethylbenzene is an inducer of liver microsomal enzymes. It is not mutagenic or teratogenic ... No information is available on reproductive toxicity or carcinogenicity of ethylbenzene. A guidance value of 22 mg/ cu m (5 ppm) has been calculated from animal studies. /This value would correspond to a weekly absorbed dose (daily ventilation of 20 cu m with 60% retention) of about 2000 mg./ The estimated exposure of the general population (even in the worst case situation) is below this guidance value. Long term occupational exposure to ethylbenzene concentrations estimated to be of this order of magnitude did not cause adverse health effects in workers.
[Environmental Health Criteria 186: Ethylbenzene pp. 19-20 (1996) by the International Programme on Chemical Safety (IPCS) under the joint sponsorship of the United Nations Environment Programme, the International Labour Organisation and the World Health Organization.]**QC REVIEWED**

Evidence for Carcinogenicity:

CLASSIFICATION: D; not classifiable as to human carcinogenicity. BASIS FOR CLASSIFICATION: nonclassifiable due to lack of animal bioassays and human studies. HUMAN CARCINOGENICITY DATA: None. ANIMAL CARCINOGENICITY DATA: None.
[U.S. Environmental Protection Agency's Integrated Risk Information System (IRIS) on Ethylbenzene (100-41-4) Available from: http://www.epa.gov/ngispgm3/iris on the Substance File List as of March 15, 2000]**PEER REVIEWED**

Human Toxicity Excerpts:

PROLONGED EXPOSURE TO ... VAPORS MAY RESULT IN FUNCTIONAL DISORDERS, INCREASE IN DEEP REFLEXES, IRRITATION OF UPPER RESPIRATORY TRACT, HEMATOLOGICAL DISORDERS (LEUKOPENIA AND LYMPHOCYTOSIS, IN PARTICULAR) AND ... HEPATOBILIARY COMPLAINTS.
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office,

1983. 2114]**PEER REVIEWED**

... ASPIRATION OF EVEN A SMALL AMT OF ETHYLBENZENE MAY CAUSE SEVERE INJURY, SINCE ITS LOW VISCOSITY AND SURFACE TENSION WILL CAUSE IT TO SPREAD OVER A LARGE SURFACE OF PULMONARY TISSUE. ...
[Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965. 92]**PEER REVIEWED**

Produces an irritant effect from chronic inhalation at 100 ppm (0.492 mg/L)/8 hr. /From table/
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1344]**PEER REVIEWED**

... /IT HAS BEEN/ SHOWN THAT CONCN OF 1 MG/L & EVEN 0.1 MG/L MAY BE DANGEROUS & MAY PRODUCE FUNCTIONAL & ORGANIC DISTURBANCES (NERVOUS SYSTEM DISORDERS, TOXIC HEPATITIS & UPPER RESP TRACT COMPLAINTS). CONCN AS LOW AS 0.01 MG/L MAY LEAD TO ... INFLAMMATION OF UPPER RESP TRACT MUCOSA.
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 2114]**PEER REVIEWED**

Ethyl benzene vapor has a transient irritant effect on human eyes at 200 ppm in air. At 1000 ppm on the first exposure it is very irritating and causes tearing, but tolerance rapidly develops. At 2000 ppm eye irritation and lacrimation are immediate and severe; 5000 ppm causes intolerable irritation of the eyes and nose.
[Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986. 413]**PEER REVIEWED**

ETHYLBENZENE IS MORE VOLATILE THAN STYRENE AND ITS MANUFACTURE IS ACCOMPANIED BY A GREATER HAZARD OF ACUTE POISONING. ...
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 2114]**PEER REVIEWED**

Skin, Eye and Respiratory Irritations:

... CHARACTERIZED ... AS MOST SEVERE IRRITANT OF THE BENZENE SERIES.
[American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices. 5th ed. Cincinnati, OH:American Conference of Governmental Industrial Hygienists, 1986. 244]**PEER REVIEWED**

A concn of 200 ppm causes eye irritation. A concn of 100 ppm for 8 hr caused irritative effects in a human.
[Cleland, J.G., G.L. Kingsbury. Multimedia Environmental Goals for Environmental Assessment. Volume 1. EPA-600/7-77-136a. Research Triangle Park, NC: EPA, Nov. 1977.,p. E-148]**PEER REVIEWED**

EXPOSURE TO CONCN OF 5000 PPM /24.6 MG/L/ ... CAUSES INTOLERABLE IRRITATION OF

EYES, MUCOUS MEMBRANES & NOSE.
[Patty, F. (ed.). Industrial Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New York: Interscience Publishers, 1963. 1232]**PEER REVIEWED**

HAZARD WARNING: ... exposure to 21.5 g/cu m (5000 ppm) ethylbenzene for a few seconds gives intolerable irritation of nose, eyes, and throat.
[Environmental Health Criteria 186: Ethylbenzene pp. 67 (1996) by the International Programme on Chemical Safety (IPCS) under the joint sponsorship of the United Nations Environment Programme, the International Labour Organisation and the World Health Organization.]**QC REVIEWED**

Medical Surveillance:

... EMPLOYMENT EXAMINATION SHOULD ENSURE THAT PERSONS WITH LIVER, KIDNEY, NERVOUS SYSTEM, BLOOD AND HEMOPOIETIC-ORGAN DISORDERS ARE /PROTECTED FROM EXPOSURE/ ... WOMEN WITH OVULATION AND MENSTRUAL CYCLE DISORDERS SHOULD ALSO BE /PROTECTED/.
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 2114]**PEER REVIEWED**

Consider the points of attack (eyes, upper respiratory system, skin, central nervous system) in placement and periodic physical examinations.
[Sittig, M. Handbook of Toxic and Hazardous Chemicals and Carcinogens, 1985. 2nd ed. Park Ridge, NJ: Noyes Data Corporation, 1985. 413]**PEER REVIEWED**

Populations at Special Risk:

IN PERSONS WITH IMPAIRED PULMONARY FUNCTION, ESP THOSE WITH OBSTRUCTIVE AIRWAY DISEASES, BREATHING ETHYL BENZENE MIGHT CAUSE EXACERBATION OF SYMPTOMS DUE TO ITS IRRITANT PROPERTIES OR PSYCHIC REFLEX BRONCHOSPASM.
[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) PublicationNo. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981.]**PEER REVIEWED**

PERSONS WITH ... EXISTING SKIN DISORDERS MAY BE MORE SUSCEPTIBLE TO EFFECTS. ...
[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) PublicationNo. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981.]**PEER REVIEWED**

... PERSONS WITH LIVER, KIDNEY, NERVOUS SYSTEM, BLOOD AND HEMOPOIETIC-ORGAN DISORDERS. ... WOMEN WITH OVULATION AND MENSTRUAL CYCLE DISORDERS. ...

[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 2114]**PEER REVIEWED**

Probable Routes of Human Exposure:

NIOSH (NOES Survey 1981-1983) has statistically estimated that 80,726 workers (21,785 of these are female) are potentially exposed to ethylbenzene in the US(1). Occupational exposure to ethylbenzene may occur via inhalation at municipal waste composting facilities where the air concn was found to be 78,000-178,000 ug/cu m(2),and through inhalation and dermal contact with this compound at worplaces where ethylbenzene is produced or used(SRC). The general population may be exposed to ethylbenzene via inhalation of ambient air, ingestion of foods and fish, and drinking contaminated water, and dermal contact with this compound and other products such as gasoline which contains ethylbenzene(SRC).
[(1) NIOSH; National Occupational Exposure Survey (NOES) (1983) (2) Eitzer BD; Environ Sci Technol 29: 896-902 (1995)]**PEER REVIEWED**

Body Burden:

Ethylbenzene was detected, not quantified, in 8 of 8 samples of mother's milk from 4 US urban areas(1). 16.5% of 387 expired air samples taken from 54 normal, healthy, urban volunteers were positive for ethylbenzene concn with an avg of 1.8 ng/l expired air(2). Whole blood samples from 250 subjects ranged in ethylbenzene concns from not detected to 59 ppb, with an avg of 1.0 ppb(3).
[(1) Pellizzari ED et al; Bull Environ Contam Toxicol 28: 322-8 (1982) (2) Krotoszynski BK et al; J Anal Toxicol 3: 225-34 (1979) (3) Antoine SR et al; Bull Environ Contam Toxicol 36: 364-71 (1986)]**PEER REVIEWED**

Average Daily Intake:

AIR INTAKE: (assume air concn of 0.2-2.7 ppb)(2-6); 17-235 ug; WATER INTAKE: (assume water concn of 0-4 ppb(1)) 0-8 ug; FOOD INTAKE: insufficient data(SRC).
[(1) Konasewich D et al; Status Report on Organic and Heavy Metal Contaminants in the Lake Erie, Michigan, Huron and Superior Basins. Great Lakes Quality Review Board (1978) (2) Arnts RR, Meeks SA; Biogenic Hydrocarbon Contribution to the Ambient Air of Selected Areas p. 31 USEPA-600/3-80-023 (1980) (3) Atshuller AP et al; Environ Sci Technol 5: 1009-16 (1981) (4) Lonneman WA et al; Environ Sci Technol 2: 1017-20 (1968) (5) Singh HB et al; Atmos Environ 15: 601-12 (1981) (6) Singh HB et al; Atmospheric Measurements of Selected Toxic Organic Chemicals USEPA-600/3-80-072 (1980)]**PEER REVIEWED**

Emergency Medical Treatment:

Emergency Medical Treatment:

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The following Overview, *** ETHYLBENZENE ***, is relevant for this HSDB record chemical.

Life Support:

- This overview assumes that basic life support measures have been instituted.

Clinical Effects:

SUMMARY OF EXPOSURE

0.2.1.1 ACUTE EXPOSURE

- Ethylbenzene is an eye, skin, and mucous membrane irritant. Narcosis may also occur.
- Exposure to ethylbenzene at significant concentrations may cause profuse lacrimation, conjunctivitis, nasal and respiratory tract irritation, chest constriction, vertigo, headache, irritability, and possibly functional nervous system disturbances at high concentrations.
- Chronic exposure in humans may caused fatigue, sleepiness, headache, and irritation of the eyes and respiratory tract.
- In experimental animals, exposure to ethylbenzene may cause eye, skin, and mucous membrane irritation; changes in liver and kidney weights; CNS depression; pulmonary edema; and respiratory failure.

HEENT

0.2.4.1 ACUTE EXPOSURE

- Ethylbenzene can be an eye irritant.

RESPIRATORY

0.2.6.1 ACUTE EXPOSURE

- Ethyl benzene is a respiratory tract irritant and is a pulmonary aspiration hazard following large ingestions. In fatal cases, pulmonary edema had developed; death occurs in respiratory failure. However, human studies demonstrated no signs or symptoms of respiratory tract irritation at 85 and 100 ppm.

NEUROLOGIC

0.2.7.1 ACUTE EXPOSURE

- Ethyl benzene has CNS depressant (narcotic) properties

at high concentrations.
- CNS symptoms may include headache, nausea, weakness, incoordination, dizziness, sleepiness, loss of coordination, judgement, and consciousness, and coma or death may occur with significant exposure. Cerebral edema may occur in fatal poisonings.

GASTROINTESTINAL

0.2.8.1 ACUTE EXPOSURE

- Ethyl benzene is a pulmonary aspiration hazard following ingestion, and is toxic with ingestion exposure. Ingestion would be predicted to cause GI tract irritation or burns.

HEPATIC

0.2.9.1 ACUTE EXPOSURE

- Slight changes in the liver occurred in rats exposed to 600 ppm for up to 16 weeks.

GENITOURINARY

0.2.10.1 ACUTE EXPOSURE

- Slight changes in the kidneys occurred in rats exposed to 600 ppm for up to 16 weeks.

HEMATOLOGIC

0.2.13.1 ACUTE EXPOSURE

- Ethyl benzene has been shown NOT to have the myelotoxic activity associated with BENZENE.

DERMATOLOGIC

0.2.14.1 ACUTE EXPOSURE

- Dermal contact causes inflammation and erythema. Ethyl benzene can be absorbed through intact skin.

REPRODUCTIVE HAZARDS

- Ethyl benzene is teratogenic and fetotoxic in experimental animals, and has been detected in umbilical cord blood.

Laboratory:

- Urinary levels of mandelic acid can be used as an indicator of exposure to ethylbenzene.

Treatment Overview:

SUMMARY EXPOSURE

- FIRST AID (NIOSH, 2000) -
  1. EYE EXPOSURE - Immediately wash the eyes with large amounts of water, occasionally lifting the lower and upper lids. Get medical attention immediately. Contact lenses should not be worn when working with this chemical.
  2. DERMAL EXPOSURE - Flush the contaminated skin with water promptly. If this chemical penetrates the clothing, immediately remove the clothing and flush the skin with water promptly. If irritation persists after washing, get medical attention.
  3. INHALATION EXPOSURE - Move the exposed person to fresh air at once. If breathing has stopped, perform mouth-to-mouth resuscitation. Keep the affected person warm and at rest. Get medical attention as soon as possible.
  4. ORAL EXPOSURE - If this chemical has been swallowed, get medical attention immediately.
  5. TARGET ORGANS - Eyes, skin, respiratory tract, and central nervous system.
- GENERAL -
  1. Move victims of inhalation exposure from the toxic environment and administer 100% humidified supplemental oxygen with assisted ventilation as required. Exposed skin and eyes should be copiously flushed with water. Because of the potential for rapid onset of CNS depression or seizures with possible aspiration of gastric contents, EMESIS SHOULD NOT BE INDUCED. Cautious gastric lavage followed by administration of activated charcoal may be of benefit if the patient is seen soon after the exposure.
- INHALATION EXPOSURE -
  1. DECONTAMINATION: Move patient to fresh air. Monitor for respiratory distress. If cough or difficulty in breathing develops, evaluate for respiratory tract irritation, bronchitis, or pneumonitis. Administer 100 percent humidified supplemental oxygen with assisted ventilation as required.
  2. If bronchospasm and wheezing occur, consider treatment with inhaled sympathomimetic agents.
  3. PULMONARY EDEMA (NONCARDIOGENIC): Maintain ventilation and oxygenation and evaluate with frequent arterial blood gas or pulse oximetry monitoring. Early use of

PEEP and mechanical ventilation may be needed.

- DERMAL EXPOSURE -
  1. DECONTAMINATION: Wash exposed area extremely thoroughly with soap and water. A physician may need to examine the area if irritation or pain persists.
  2. Treat dermal irritation or burns with standard topical therapy. Patients developing dermal hypersensitivity reactions may require treatment with systemic or topical corticosteroids or antihistamines.
  3. Some chemicals can produce systemic poisoning by absorption through intact skin. Carefully observe patients with dermal exposure for the development of any systemic signs or symptoms and administer symptomatic treatment as necessary.
- EYE EXPOSURE -
  1. DECONTAMINATION: Exposed eyes should be irrigated with copious amounts of tepid water for at least 15 minutes. If irritation, pain, swelling, lacrimation, or photophobia persist, the patient should be seen in a health care facility.
- ORAL EXPOSURE -
  1. Because of the potential for CNS depression or gastrointestinal tract irritation, do not induce emesis.
  2. Weigh the potential toxicity of the amount of ethylbenzene ingested against the substantial risk of pulmonary aspiration of gastric contents. Ethylbenzene may "wick" up around a lavage tube, allowing pulmonary aspiration.
     a. Significant esophageal or gastrointestinal tract irritation or burns may occur following ingestion. The possible benefit of early removal of some ingested material by cautious gastric lavage must be weighed against potential complications of bleeding or perforation.
  3. GASTRIC LAVAGE: Consider after ingestion of a potentially life-threatening amount of poison if it can be performed soon after ingestion (generally within 1 hour). Protect airway by placement in Trendelenburg and left lateral decubitus position or by endotracheal intubation. Control any seizures first.
     a. CONTRAINDICATIONS: Loss of airway protective reflexes or decreased level of consciousness in unintubated patients; following ingestion of corrosives; hydrocarbons (high aspiration potential); patients at risk of hemorrhage or gastrointestinal perforation;

and trivial or non-toxic ingestion.

4. ACTIVATED CHARCOAL/CATHARTIC: Administer charcoal slurry, aqueous or mixed with saline cathartic or sorbitol. The FDA suggests 240 mL of diluent/30 g of charcoal. Usual charcoal dose is 25 to 100 grams in adults and adolescents, 25 to 50 grams in children (1 to 12 years old), and 1 gram/kilogram in infants less than 1 year old.
   a. Routine use of cathartics is NOT recommended. If used, administer only ONE dose of cathartic. Administer one dose of a cathartic, mixed with charcoal or given separately. See "Treatment: Prevention of Absorption" in the main document.
5. Observe patients with ingestion carefully for the possible development of esophageal or gastrointestinal tract irritation or burns. If signs or symptoms of esophageal irritation or burns are present, consider endoscopy to determine the extent of injury.

ORAL EXPOSURE

- Because of the potential for CNS depression or gastrointestinal tract irritation, Do NOT induce emesis.
- Weigh the potential toxicity of the amount of ethylbenzene ingested against the substantial risk of aspiration. Ethylbenzene may "wick" up around a lavage tube, allowing pulmonary aspiration.
  1. Significant esophageal or gastrointestinal tract irritation or burns may occur following ingestion. The possible benefit of early removal of some ingested material by cautious gastric lavage must be weighed against potential complications of bleeding or perforation.
- GASTRIC LAVAGE: Consider after ingestion of a potentially life-threatening amount of poison if it can be performed soon after ingestion (generally within 1 hour). Protect airway by placement in Trendelenburg and left lateral decubitus position or by endotracheal intubation. Control any seizures first.
  1. CONTRAINDICATIONS: Loss of airway protective reflexes or decreased level of consciousness in unintubated patients; following ingestion of corrosives; hydrocarbons (high aspiration potential); patients at risk of hemorrhage or gastrointestinal perforation; and trivial or non-toxic ingestion.
- ACTIVATED CHARCOAL/CATHARTIC: Administer charcoal slurry, aqueous or mixed with saline cathartic or sorbitol. The FDA suggests 240 mL of diluent/30 g of

charcoal. Usual charcoal dose is 25 to 100 grams in adults and adolescents, 25 to 50 grams in children (1 to 12 years old), and 1 gram/kilogram in infants less than 1 year old.

1. Routine use of cathartics is NOT recommended. If used, administer only ONE dose of cathartic. Administer one dose of a cathartic, mixed with charcoal or given separately. See "Treatment: Prevention of Absorption" in the main document.

- Observe patients with ingestion carefully for the possible development of esophageal or gastrointestinal tract irritation or burns. If signs or symptoms of esophageal irritation or burns are present, consider endoscopy to determine the extent of injury.

INHALATION EXPOSURE

- DECONTAMINATION: Move patient to fresh air. Monitor for respiratory distress. If cough or difficulty in breathing develops, evaluate for respiratory tract irritation, bronchitis, or pneumonitis. Administer 100 percent humidified supplemental oxygen with assisted ventilation as required.
- If bronchospasm and wheezing occur, consider treatment with inhaled sympathomimetic agents.
- PULMONARY EDEMA (NONCARDIOGENIC): Maintain ventilation and oxygenation and evaluate with frequent arterial blood gas or pulse oximetry monitoring. Early use of PEEP and mechanical ventilation may be needed.

EYE EXPOSURE

- DECONTAMINATION: Exposed eyes should be irrigated with copious amounts of tepid water for at least 15 minutes. If irritation, pain, swelling, lacrimation, or photophobia persist, the patient should be seen in a health care facility.

DERMAL EXPOSURE

- DECONTAMINATION: Wash exposed area extremely thoroughly with soap and water. A physician may need to examine the area if irritation or pain persists.
- Treat dermal irritation or burns with standard topical therapy. Patients developing dermal hypersensitivity reactions may require treatment with systemic or topical corticosteroids or antihistamines.
- Some chemicals can produce systemic poisoning by absorption through intact skin. Carefully observe patients with dermal exposure for the development of any systemic signs or symptoms and administer symptomatic treatment as necessary.

[Rumack BH: POISINDEX(R) Information System. Micromedex, Inc., Englewood, CO, 2001; CCIS Volume 107, edition exp February, 2001. Hall AH & Rumack BH (Eds):TOMES(R) Information System. Micromedex, Inc., Englewood, CO, 2001; CCIS Volume 107, edition exp February, 2001.] **PEER REVIEWED**

Antidote and Emergency Treatment:

Basic treatment: Establish a patent airway. Suction if necessary. Watch for signs of respiratory insufficiency and assist ventilations if necessary. Administer oxygen by nonrebreather mask at 10 to 15 L/min. Monitor for pulmonary edema and treat if necessary ... . Monitor for shock and treat if necessary ... . For eye contamination, flush eyes immediately with water. Irrigate each eye continuously with normal saline during transport ... . Do not use emetics. For ingestion, rinse mouth and administer 5 ml/kg up to 200 ml of water for dilution if the patient can swallow, has a strong gag reflex, and does not drool. Administer activated charcoal ... . /Aromatic hydrocarbons and related compounds/
[Bronstein, A.C., P.L. Currance; Emergency Care for Hazardous Materials Exposure. 2nd ed. St. Louis, MO. Mosby Lifeline. 1994.,p. 181-2]**PEER REVIEWED**

Advanced treatment: Consider orotracheal or nasotracheal intubation for airway control in the patient who is unconscious or in respiratory arrest. Positive-pressure ventilation techniques with a bag-valve-mask device may be beneficial. Monitor cardiac rhythm and treat arrhythmias if necessary ... . Start an IV with D5W /SRP: "To keep open", minimal flow rate/. Use lactated Ringer's if signs of hypovolemia are present. Watch for signs of fluid overload. Consider drug therapy for pulmonary edema ... . Treat seizures with diazepam (Valium) ... . Use proparacaine hydrochloride to assist eye irrigation ... . /Aromatics hydrocarbons and related compounds/
[Bronstein, A.C., P.L. Currance; Emergency Care for Hazardous Materials Exposure. 2nd ed. St. Louis, MO. Mosby Lifeline. 1994. 182]**PEER REVIEWED**

Animal Toxicity Studies:

Toxicity Summary:

The acute toxicity of ethylbenzene to algae, aquatic invertebrates and fish is moderate. ... No information is available regarding chronic exposure of aquatic organisms to ethylbenzene. There is limited information regarding the toxicity of ethylbenzene to bacteria ... There are no data for terrestrial plants, birds, or wild mammals. Human exposure to ethylbenzene occurs mainly by inhalation; 40-60% of inhaled ethylbenzene is retained in the lung. Ethylbenzene is extensively metabolized, mainly to mandelic and phenylglyoxylic acids. These urinary metabolites can be used to monitor human exposures. Ethylbenzene has low acute and chronic toxicity for both animals and humans. It is toxic to the central nervous system and is an irritant of mucous membranes and the eyes. ... Ethylbenzene is an inducer of liver microsomal enzymes. It is not mutagenic or teratogenic ... No information is available on reproductive toxicity or carcinogenicity of ethylbenzene. A guidance value of 22 mg/ cu m (5 ppm) has been calculated from animal studies. /This value would correspond to a weekly absorbed dose (daily ventilation of 20 cu m with 60% retention) of about 2000 mg./ The estimated exposure of the general

population (even in the worst case situation) is below this guidance value. Long term occupational exposure to ethylbenzene concentrations estimated to be of this order of magnitude did not cause adverse health effects in workers.
[Environmental Health Criteria 186: Ethylbenzene pp. 19-20 (1996) by the International Programme on Chemical Safety (IPCS) under the joint sponsorship of the United Nations Environment Programme, the International Labour Organisation and the World Health Organization.]**QC REVIEWED**

Evidence for Carcinogenicity:

CLASSIFICATION: D; not classifiable as to human carcinogenicity. BASIS FOR CLASSIFICATION: nonclassifiable due to lack of animal bioassays and human studies. HUMAN CARCINOGENICITY DATA: None. ANIMAL CARCINOGENICITY DATA: None.
[U.S. Environmental Protection Agency's Integrated Risk Information System (IRIS) on Ethylbenzene (100-41-4) Available from: http://www.epa.gov/ngispgm3/iris on the Substance File List as of March 15, 2000]**PEER REVIEWED**

Non-Human Toxicity Excerpts:

... From ingestion of or exposure of skin or lung to high concns causes /CNS depression/ in animals. Although similar to benzene, ethylbenzene apparently does not cause bone marrow problems.
[Friberg, L., Nordberg, G.F., Kessler, E. and Vouk, V.B. (eds). Handbook of the Toxicology of Metals. 2nd ed. Vols I, II.: Amsterdam: Elsevier Science Publishers B.V., 1986. 288]**PEER REVIEWED**

EXPOSURE OF GUINEA PIGS TO 1% CONCENTRATION HAS BEEN REPORTED AS CAUSING ATAXIA, LOSS OF CONSCIOUSNESS, TREMOR OF THE EXTREMITIES, AND FINALLY DEATH THROUGH RESPIRATORY FAILURE. THE PATHOLOGICAL FINDINGS WERE CONGESTION OF THE BRAIN AND LUNGS WITH EDEMA.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1522]**PEER REVIEWED**

... CONCN ... OVER 2 MG/L MAY CAUSE ACUTE POISONING /IN LABORATORY ANIMALS/ ... INITIAL SYMPTOMS ... INCL IRRRTATION OF MUCOUS MEMBRANES ... FOLLOWED BY ... /CNS DEPRESSION/, CRAMPS & DEATH ... DUE TO RESPIRATORY-CENTER PARALYSIS. MAIN PATHOLOGICAL FINDINGS ARE MARKED EDEMA OF BRAIN & LUNG, FOCI OF EPITHELIAL NECROSIS IN RENAL TUBULES & HEPATIC DYSTROPHY.
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 2114]**PEER REVIEWED**

... /GUINEA PIGS/ THAT DIED FROM EXPOSURE /TO 10000 PPM FOR FEW MIN OR 5000 PPM FOR 30-60 MIN/ HAD INTENSE CONGESTION AND EDEMA OF LUNG AND GENERALIZED VISCERAL HYPEREMIA.
[Browning, E. Toxicity and Metabolism of Industrial Solvents. New

York: American Elsevier, 1965. 91]**PEER REVIEWED**

IN GUINEA PIGS, 0.3% BY VOL IS MAX AMT FOR 1 HR WITHOUT SERIOUS SYMPTOMS; 0.1% BY VOL IS MAX AMT FOR SEVERAL HR WITHOUT SERIOUS DISTURBANCES. /FROM TABLE/
[Patty, F. (ed.). Industrial Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New York: Interscience Publishers, 1963. 1232]**PEER REVIEWED**

REPEATED APPLICATIONS OF UNDILUTED ETHYLBENZENE TO THE SKIN OF RABBITS CAUSED ... BLISTERING.
[Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965. 92]**PEER REVIEWED**

... RATS, RABBITS, GUINEA PIGS, AND MONKEYS /WERE EXPOSED/ TO CONCN OF ... 400-2200 PPM, 7 TO 8 HR/DAY, 5 DAYS A WK FOR AS LONG AS 6 MONTHS. THE GUINEA PIGS, RABBITS, AND MONKEYS WERE NOT AFFECTED ... SLIGHT INCREASE IN AVG WT OF KIDNEYS AND LIVERS WERE OBSERVED IN RATS EXPOSED TO 400 PPM FOR 186 DAYS.
[Patty, F. (ed.). Industrial Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New York: Interscience Publishers, 1963. 1232]**PEER REVIEWED**

... RATS /WERE INJECTED/ SUBCUTANEOUSLY WITH 1 ML ... PER KG OF BODY WT DAILY FOR 2 WEEKS AND ... NO DECREASE IN THE TOTAL FEMORAL MARROW NUCLEATED CELL COUNT /WAS OBSERVED/. THESE ANIMALS DEVELOPED A LEUCOCYTOSIS INSTEAD OF SEVERE LEUCOPENIAS FOUND IN BENZENE-DOSED ANIMALS WHICH SERVED AS POSITIVE CONTROLS.
[Patty, F. (ed.). Industrial Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New York: Interscience Publishers, 1963. 1232]**PEER REVIEWED**

EXPOSURE TO 2000 PPM FOR UP TO 375 MIN CAUSED IN SOME OF /GUINEA PIGS/ ... MOTOR ATAXIA AND APPARENT UNCONSCIOUSNESS; WITH 10,000 PPM THIS STAGE WAS REACHED IN 18 MIN. IT WAS PRECEDED BY VERTIGO, UNSTEADINESS AND ATAXIA.
[Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965. 92]**PEER REVIEWED**

LIVER & KIDNEY WT INCREASED IN RATS GIVEN SUBCHRONIC ORAL DOSES OF 408-680 MG/KG/DAY FOR 182 DAYS. /FROM TABLE/
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1345]**PEER REVIEWED**

INHALATION @ 3050 PPM (15 MG/L) PRODUCED LOSS OF RIGHTING RESPONSE IN MICE & DEATH IN 2 HR FROM 9150 PPM (45 MG/L). IN GUINEA PIGS 1000 PPM (4.92 MG/L)/3 MIN PRODUCED SLIGHT NASAL IRRITATION, @ 8 MIN EYE IRRITATION; 2000 PPM (9.84 MG/L)/1 MIN PRODUCED MODERATE EYE & NASAL IRRITATION, UNCONSCIOUSNESS @ 345 MIN.

/FROM TABLE/
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1344]**PEER REVIEWED**

SUBACUTE EXPOSURE OF MALE RATS TO 2000 PPM PRODUCED INCREASES OF DOPAMINE & NORADRENALINE LEVELS & TURNOVER IN VARIOUS PARTS OF HYPOTHALAMUS & MEDIAN EMINENCE 16-18 HR FOLLOWING LAST EXPOSURE.
[ANDERSON K ET AL, TOXICOL APPL PHARMACOL 60 (3): 535 (1981)]**PEER REVIEWED**

Rats inhaling 600, 1200, or 2400 mg ethylbenzene/cu m for 24 hr/day from days 7-15 of pregnancy showed mild toxicity. The highest dose retarded skeletal development and weight gain in the fetuses and increased the incidence of extra ribs. Sacral displacement with abnormal development was observed in 2 instances. Thus, ethylbenzene, has some embryotoxic and teratogenic activity.
[Tatrai E et al; Egeszsegtudomany 26 (3): 297-303 (1982)]**PEER REVIEWED**

Ethylbenzene was investigated ... as a sensory irritant in mice. The concn necessary to depress the respiratory rate by 50% (RD 50) due to sensory irritation of the upper respiratory tract was 4060 ppm. ... A model for the sensory irritating action ... was proposed on the basis of ... physical interaction with a receptor protein.
[Nielsen GD, Alarie Y; Toxical Appl Pharmacol 65 (3): 459-77 (1982)]**PEER REVIEWED**

Drop application to rabbit eyes caused slight irritation and no corneal injury demonstrable by fluorescein staining. Standard testing on rabbit eyes gave an injury grade of 2 on a scale of 10.
[Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986. 413]**PEER REVIEWED**

Rats were exposed for 3 days by inhalation to 2000 ppm of a xylene mixture, or ... ethylbenzene. All solvents increased hepatic cytochrome p450 concn and NADPH-cytochrome C reductase activity. The ability of ethylbenzene to modify the metabolism of other potentially toxic substances in liver, kidney, and lung microsomes suggested the possibility of synergistic toxic responses.
[Toftgard R, Nilsen OG; Toxicol 23 (2-3): 197-212 (1982)]**PEER REVIEWED**

Concn of < 0.25 mg/l can cause tainting of fish flesh.
[Cleland, J.G., G.L. Kingsbury. Multimedia Environmental Goals for Environmental Assessment. Volume 1. EPA-600/7-77-136a. Research Triangle Park, NC: EPA, Nov. 1977.,p. E-148]**PEER REVIEWED**

Neither maternal toxicity nor embryotoxicity was observed in gravid rabbits exposed to ethylbenzene /by inhalation/ at 100 or 1000 ppm.
[NIOSH; Teratologic Assessment of Ethylbenzene and 2-Ethoxyethanol p.iii (1981) NIOSH Contract No. 210-79-0037]**PEER REVIEWED**

Neither maternal toxicity nor embyrotoxicity was observed /in pregnant rats/ exposed to ethylbenzene /by inhalation/ at 100 ppm ... but /1000 ppm/ induced some indications of toxicity. ... A significant

increase in the incidence of extra ribs was detected in rat fetuses exposed in utero to the high level.
[NIOSH; Teratologic Assessment of Ethylbenzene and 2-Ethoxyethanol p.iii (1981) NIOSH Contract No. 210-79-0037]**PEER REVIEWED**

Mice, B6C3F1 Fischer-344 rats, and /rabbits /New Zealand/ (five/sex/group) were exposed by inhalation to ethylbenzene vapors for 6 hr/day, 5 days/week for 4 weeks (20 exposures). Rats and mice received 0, 99, 382, or 782 ppm ethylbenzene while rabbits received 0, 382, 782, or 1610 ppm. No changes were evident in mortality patterns, clinical chemistries, urinalyses, or treatment-related gross/microscopic (including ophthalmologic) lesions. Rats exhibited sporadic lacrimation and salivation, as well as significantly increased liver weights at 382 and 782 ppm, and small increases in leukocyte counts at 782 ppm. Males at this exposure level also showed marginal elevations in platelet counts. In mice, females showed statistically increased absolute and relative liver weights at 382 and 782 ppm while males had statistically increased relative liver-to-brain weight ratios only at 782 ppm. Female rabbits at the high exposure level of 1610 ppm gained weight more slowly than controls (not statistically significant); males showed a similar transient downward trend after 1 week, but showed no differences from controls at study's end. A no observed adverse effect level (NOAEL) of 382 ppm appears appropriate for rats and mice with a lowest observed adverse effect level (LOAEL) of 782 ppm. A NOAEL of 782 ppm and LOAEL of 1610 ppm are appropriate for rabbits.
[Cragg ST et al; Fundam Appl Toxicol 13 (3): 399-408 (1989)]**PEER REVIEWED**

Repeated application of undiluted ethyl benzene to the ear and shaved abdominal area of rabbits (10-20 applications over a period of 2-4 wk) resulted in erthyema, edema, and superficial necrosis. ... Two drops of ethyl benzene into the conjunctival sac produced only a slight irritation of the conjunctival membranes but no corneal injury.
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Volumes I,II, III. Cincinnati, OH: ACGIH, 1991. 581]**PEER REVIEWED**

Inhalation of 2600 mg/cu m (600 ppm) ethyl benzene 7 hr/day, 5 days/wk for 186 days caused degeneration of the germinal epithelium in the testes of rabbits and monkeys but not of rats. Pregnant rats exposed at 100 or 1000 ppm 6 hr/day for 3 wk prior to mating and on days 1-19 of gestation had pups with a significant increase ($p < 0.05$) in extra rib formation; at the higher dose, maternal toxicity was indicated by increased liver, kidney, and spleen weights.
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Volumes I,II, III. Cincinnati, OH: ACGIH, 1991. 582]**PEER REVIEWED**

... CONCLUSIONS: Under the conditions of these 2 yr inhalation studies, there was clear evidence of carcinogenic activity of ethylbenzene in male F344/N rats based on incr incidences of renal tubule neoplasms. The incidences of testicular adenoma were also incr. There was some evidence of carcinogenic activity of ethylbenzene in female F344/N rats based on incr incidences of renal tubule adenomas. There was some evidence of carcinogenic activity of ethylbenzene in male B6C3F1 mice based on incr incidences of alveolar/bronchiolar neoplasms. There was some evidence of carcinogenic activity of ethylbenzene in female B6C3F1 mice based on incr incidences of hepatocellular neoplasms.

[Toxicology & Carcinogenesis Studies of Ethylbenzene in F344/N Rats and B6C3F1 Mice p.5 Technical Report Series No. 466 (1999) NIH Publication No. 99-3956 U.S. Department of Health and Human Services, National Toxicology Program, National Institute of Environmental Health Sciences, Research Triangle Park, NC 27709]**PEER REVIEWED**

National Toxicology Program Studies:

... 2 Yr Study in Rats: Groups of 50 male and 50 female F344/N rats were exposed to 0, 75, 250 or 750 ppm ethylbenzene 6 hr day, 5 days/wk for 104 wk. ... 2 Yr Study in Mice: Groups of 50 male and 50 female B6C3F1 mice were exposed to 0, 75, 250 or 750 ppm ethylbenzene by inhalation, 6 hr/day, 5 days/wk for 103 wk. ... CONCLUSIONS: Under the conditions of these 2 yr inhalation studies, there was clear evidence of carcinogenic activity of ethylbenzene in male F344/N rats based on incr incidences of renal tubule neoplasms. The incidences of testicular adenoma were also incr. There was some evidence of carcinogenic activity of ethylbenzene in female F344/N rats based on incr incidences of renal tubule adenomas. There was some evidence of carcinogenic activity of ethylbenzene in male B6C3F1 mice based on incr incidences of alveolar/bronchiolar neoplasms. There was some evidence of carcinogenic activity of ethylbenzene in female B6C3F1 mice based on incr incidences of hepatocellular neoplasms.
[Toxicology & Carcinogenesis Studies of Ethylbenzene in F344/N Rats and B6C3F1 Mice p.5 Technical Report Series No. 466 (1999) NIH Publication No. 99-3956 U.S. Department of Health and Human Services, National Toxicology Program, National Institute of Environmental Health Sciences, Research Triangle Park, NC 27709]**QC REVIEWED**

Non-Human Toxicity Values:

LD50 Rat oral 5.46 g/kg.
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 643]**PEER REVIEWED**

LD50 Rat oral 3500 mg/kg
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1522]**PEER REVIEWED**

LD50 Mouse ip 2272 mg/kg
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1522]**PEER REVIEWED**

LD50 Rabbit skin 17,800 mg/kg
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1522]**PEER REVIEWED**

Ecotoxicity Values:

LC50 Lepomis macrochirus 32 mg/l/96 hr /Conditions of bioassay not specified/

[Pickering QH, Henderson C; J Water Pollut Control Fed 38: 1419 (1966)]**PEER REVIEWED**

LC50 Carassius auratus 94.44 mg/l/96 hr /Conditions of bioassay not specified/
[Pickering QH, Henderson C; J Water Pollut Control Fed 38: 1419 (1966)]**PEER REVIEWED**

LC50 Lebistes reticulatus 97.10 mg/l/96 hr /Conditions of bioassay not specified/
[Pickering QH, Henderson C; J Water Pollut Control Fed 38: 1419 (1966)]**PEER REVIEWED**

LC50 Mysidopsis bahia (shrimp) 87.6 mg/l 96 hr in a static unmeasured bioassay
[USEPA; In-depth Studies on Health Environmental Impacts of Selected Water Pollutants (1978) EPA No 68-01-4646]**PEER REVIEWED**

LC50 Cyprinodon variegatus (sheepshead minnow) 275 mg/l 96 hr in a static unmeasured bioassay
[USEPA; In-depth Studies on Health Environmental Impacts of Selected Water Pollutants (1978) EPA No 68-01-4646]**PEER REVIEWED**

LC50 Pimephales promelas (fathead minnow) 42.3 (hardwater) to 48.5 (softwater) mg/l 96 hr /Conditions of bioassay not specified/
[Pickering OH, Henderson C; J Water Pollut Control Fed 38: 1419 (1966)]**PEER REVIEWED**

LC50 Poecilla reticulata (guppy) 97.1 mg/l/96 hr /Conditions of bioassay not specified/
[Pickering OH, Henderson C; J Water Pollut Control Fed 38: 1419 (1966)]**PEER REVIEWED**

Toxicity threshold (cell multiplication inhibition test): Microcystis aeruginosa (algae) 33 mg/l; Scenedesmus quadricauda (green algae) > 160 mg/l
[Verschueren, K. Handbook of Environmental Data on Organic Chemicals. 3rd ed. New York, NY: Van Nostrand Reinhold Co., 1996. 946]**PEER REVIEWED**

Toxicity threshold (cell multiplication inhibition test): Entosiphon sulcatum (protozoa) 140 mg/l; Uronema parduczi Chatton-Lwoff (protozoa) > 110 mg/l.
[Verschueren, K. Handbook of Environmental Data on Organic Chemicals. 3rd ed. New York, NY: Van Nostrand Reinhold Co., 1996. 946]**PEER REVIEWED**

Toxicity threshold (cell multiplication inhibition test): Pseudomonas putida (bacteria) 12 mg/l.
[Verschueren, K. Handbook of Environmental Data on Organic Chemicals. 3rd ed. New York, NY: Van Nostrand Reinhold Co., 1996. 946]**PEER REVIEWED**

LC50 Palaemonetes pugio (grass shrimp, adult) 14,400 ug/l/24 hr in a static unmeasured bioassay
[USEPA; Ambient Water Quality Criteria Doc: Ethylbenzene p.3-7 (1980) EPA 440/5-80-048]**PEER REVIEWED**

LC50 Palaemonetes pugio (grass shrimp, larva) 10,200 ug/l/24 hr in a static unmeasured bioassay

[USEPA; Ambient Water Quality Criteria Doc: Ethylbenzene p.3-7 (1980) EPA 440/5-80-048]**PEER REVIEWED**

LC50 Pimephales promelas (fathead minnow) 12.1 mg/l/96 hr (confidence limit 11.5 - 12.7 mg/l), flow-through bioassay with measured concentrations, 26.1 deg C, dissolved oxygen 7.0 mg/l, hardness 45.6 mg/l calcium carbonate, alkalinity 43.0 mg/l calcium carbonate, and pH 7.39.
[Geiger D.L., Poirier S.H., Brooke L.T., Call D.J., eds. Acute Toxicities of Organic Chemicals to Fathead Minnows (Pimephales Promelas). Vol. III. Superior,Wisconsin: University of Wisconsin-Superior, 1986. 189]**PEER REVIEWED**

TSCA Test Submissions:

In a single generation reproduction study, 380 female and 60 male Wistar rats were exposed to ethylbenzene at average daily concentrations of 97 or 959 ppm 7 hours per day, 5 days per week for 3 weeks. They were then mated and exposed daily on gestation days (GD) 1-19 at concentrations of 96 (low) or 985 (high) ppm. Animals were sacrificed and examined on GD 21. No significant differences were observed between treatment groups and controls in food consumption, gestational body weights (of pregnant rats), organ weights (of male rats), histopathology of liver, kidney or lungs, percent pregnancy, no. of corpora lutea, no. of implants, total live or dead fetuses, no. of live or dead fetuses per litter, no. of resorptions per litter and percent litters with resorptions. A significant difference (ANOVA, Duncan's multiple range test) was observed in pregestational body weights in both treatment groups. Maternal toxicity was indicated in the high dose groups (dosed at the high level during both periods or dosed with air during pregestational and with the high level during gestation) by significant differences (ANOVA, Duncan's multiple range test) in liver, spleen and kidney weights. Statistically significant differences were seen in mean crown-rump length (in the group which was dosed at the high level during both periods), supernumerary ribs (in the 2 high dose groups and the group which was dosed with air pregestationally and with the low level during gestation) and rudimentary rib incidence (in the group dosed with air during pregestation and with the high level during gestation).
[Battelle Pacific Northwest Laboratories; Teratologic Assessment of Ethylbenzene and 2-Ethoxyethanol with Cover Letter Dated 061887, (1981), EPA Document No. 86870000402, Fiche No. OTS0513150] **UNREVIEWED**

In a single generation reproduction study 96 New Zealand White rabbits were artifically inseminated and exposed to ethylbenzene at average daily concentrations of 99 or 962 ppm 7 hours per day, through gestation day (GD) 24. Animals were sacrificed and examined on GD 30. Mortality was observed in 2 does, 1 from each dose group. No significant differences were observed between treatment groups and controls in the following: food consumption; body weight; weight gain; lung, kidney, and spleen mean weights; histopathology of liver, kidney, or lungs; percent pregnancy; no. of corpora lutea; no. of implants; total live or dead fetuses; no. of dead fetuses per litter; no. of resorptions per litter; percent litters with resorptions; and skeletal, visceral, or external parameters in fetuses. Significant differences (ANOVA, Duncan's multiple range test) relative to controls were observed in liver weights of the high dose group and in mean number of live fetuses per litter in both treatment groups.
[Battelle Pacific Northwest Laboratories; Teratologic Assessment of Ethylbenzene and 2-Ethoxyethanol with Cover Letter Dated 061887, (1981), EPA Document No. 86870000402, Fiche No. OTS0513150]

UNREVIEWED

Ethylbenzene (CAS# 100-41-4) was evaluated for developmental toxicity in 89, 77, and 77 female Wistar rats exposed to 0, 100, and 1000 ppm of the test material respectively by inhalation for 7 hours per day, 5 days per week for 3 weeks. They were then mated and exposed daily through the 19th day of gestation. The rats were killed and examined at the 21st day of gestation. No significant differences were observed in food consumption and body weights during progestational and gestational exposure periods. At 1000 ppm relative and absolute liver, spleen, and kidney weights were significantly greater than controls and or the 100 ppm group. No treatment-related histological changes were observed. Body weights, placenta weights, and sex ratios were all within normal limits. There were no significant increases in major malformations or minor anomalies. Litters were examined for the presence of external, visceral, and skeletal defects as well as the incidence of growth retardation and intrauterine mortality. A statistically significant increased incidence of fetal supernumary ribs was observed at the 1000 ppm exposure. It was concluded that ethylbenzene caused maternal and developmental toxicity (significant increase in extra ribs) at 1000 ppm.
[SHELL OIL CO; Teratogenic assessment of ethylbenzene and 2-ethoxyethanol; EPA 88-920002072, 1/01/81, Fiche No. OTS0539167] **UNREVIEWED**

Ethylbenzene (CAS# 100-41-4) was evaluated for developmental toxicity in 24, 23, and 22 New Zealand white rabbits artificially inseminated and exposed for 7 hours daily to 0, 100, and 1000 ppm of the test material respectively until the 24th day of gestation. Neither maternal toxicity nor embryotoxicity was observed in rabbits exposed to ethylbenzene at 100 or 1000 ppm. Rabbits had increased maternal liver weights at 1000 ppm and reduced mean number of live fetuses at 100 and 1000 ppm. No significant differences were observed in food consumption and weight gain. No treatment-related organ weight or histopathological changes were observed. Fetal size (weight and length), placenta weights, and sex ratios were all within normal limits. The sex ratios of the groups were not affected by treatment. No statistically significant incidences of major malformations, minor anomalies, or common variants were observed. It was concluded that the test material did not induce significant maternal toxicity, embryomortality, growth retardation, or teratogenicity at 1000 ppm.
[SHELL OIL CO; Teratogenic assessment of ethylbenzene and 2-ethoxyethanol; EPA 88-920002072, 1/01/81, Fiche No. OTS0539167] **UNREVIEWED**

The frequency of chromosomal aberrations was evaluated in vitro by exposing rats liver (RL1) cells to 25, 50 or 100 ug of ethyl benzene/ml. No increases in the frequency of chromatid gaps, chromatid breaks or total chromosome aberrations was observed at any dose level. Ethyl benzene did not induce chromosome damage in this assay.
[Shell Oil; In Vitro Genotoxicity Studies with Ethyl Benzene Hydroperoxide (EBHP) and Ethyl Benzene, (1981), EPA Doc. No. 86-870001656, Fiche No. OTS0515732] **UNREVIEWED**

The mutagenicity of ethyl benzene was evaluated in E. coli tester strains WP2 and WP2uvrA and in Salmonella tester strains TA98, TA100, TA1535, TA1537, and TA1538 (Ames test), both in the presence and absence of added metabolic activation by Aroclor-induced rat liver S9 fraction. Based on the results of preliminary bacterial toxicity determinations, ethyl benzene, in DMSO, was tested for mutagenicity at concentrations of 0.2, 2.0, 20.0, 200.0, and 2000.0 ug/plate using the direct plate

incorporation method. Ethyl benzene did not cause a positive response in any of the tester strains with or without metabolic activation.
[Shell Oil; In Vitro Genotoxicity Studies with Ethyl Benzene Hydroperoxide (EBHP) and Ethyl Benzene, (1981), EPA Doc. No. 86-870001656, Fiche No. OTS0515732] **UNREVIEWED**

The ability of ethyl benzene to induce conversion of differentially inactive alleles to wild-type alleles in Saccharomyces cervisiae was examined in the mitotic gene conversion assay. The cultures were dosed with solutions of 20 ul (in the absence of added metabolic action provided by Aroclor-induced rat liver S9 fraction) or 25 ul (with S9) of 1, 10, 50, 100 or 500 mg ethyl benzene/ml. Ethyl benzene did not produce an increase mitotic gene conversion, either with or without added metabolic activation, and was not considered to be mutagenic in the assay.
[Shell Oil; In Vitro Genotoxicity Studies with Ethyl Benzene Hydroperoxide (EBHP) and Ethyl Benzene, (1981), EPA Doc. No. 86-870001656, Fiche No. OTS0515732] **UNREVIEWED**

Metabolism/Pharmacokinetics:

Metabolism/Metabolites:

ETHYL BENZENE IN MAN IS METABOLIZED 64% TO MANDELIC AND 25% TO PHENYLGLYOXYLIC ACID AND EXCRETED INTO URINE.
[Thienes, C., and T.J. Haley. Clinical Toxicology. 5th ed. Philadelphia: Lea and Febiger, 1972. 126]**PEER REVIEWED**

THE OXIDATION OF ETHYLBENZENE TO METHYLPHENYLCARBINOL IN ANIMALS ... WAS CONFIRMED ... WITH ADDITIONAL FINDING THAT BOTH ISOMERS OF METHYL PHENYL CARBINOL (THE + AND - FORMS) IN EQUAL AMT ARE RESULT OF ITS BIOLOGICAL HYDROXYLATION.
[Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965. 91]**PEER REVIEWED**

In the rabbit, it is metabolized to a number of oxidation products and subsequently excreted. The major urinary metabolite is hippuric acid. The oxidation products are benzoic acid, phenylacetic acid, and mandelic acid, excreted as the glycine conjugate, and also methylphenylcarbinol, 1-phenylethanol, excreted as the glucuronide.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1343]**PEER REVIEWED**

FROM A DOSE OF 100 MG/KG ADMIN ORALLY TO RATS ... THE URINARY METABOLITES, P-ETHYLPHENOL, ABOUT 0.3%, & SMALLER QUANTITIES OF 1- & 2-PHENYLETHANOL /WERE IDENTIFIED/.
[Clayton, G. D. and F. E. Clayton (eds.). Patty's Industrial Hygiene and Toxicology: Volume 2A, 2B, 2C: Toxicology. 3rd ed. New York: John Wiley Sons, 1981-1982. 3304]**PEER REVIEWED**

URINARY SULFATE RATIO DECREASES ARE NORMALLY A ROUGH EST OF

DOSE-RELATED ALKYLBENZENE HYDROXYLATION DUE MAINLY TO SIDE CHAIN OXIDATION. ... THIS ... DOES NOT HOLD WITH DOSE-ACTION RELATIONSHIP FOR ETHYLBENZENE. ... AT HIGH DOSES, RING HYDROXYLATION INCREASES, ALTERING SULFATE RATIO.
[Clayton, G. D. and F. E. Clayton (eds.). Patty's Industrial Hygiene and Toxicology: Volume 2A, 2B, 2C: Toxicology. 3rd ed. New York: John Wiley Sons, 1981-1982. 3304]**PEER REVIEWED**

PRODUCTS OF RING HYDROXYLATION ... DETECTED FOR 1ST TIME IN RABBIT URINE. ... IDENTIFICATION OF M- & P-HYDROXYACETOPHENONE & ... ACETOPHENONE REVEALS THAT FURTHER OXIDATION IN SIDE-CHAIN OF ACETOPHENONE TO PHENACYL ALCOHOL (& THEN TO BENZOIC ACID) IS NOT ONLY PATHWAY. ... HOWEVER, RING-HYDROXYLATED PRODUCTS ARE ONLY MINOR ONES.
[The Chemical Society. Foreign Compound Metabolism in Mammals. Volume 4: A Review of the Literature Published during 1974 and 1975. London: The Chemical Society, 1977. 247]**PEER REVIEWED**

SINCE ... (1+) & (-1)METHYLPHENYL CARBINOL YIELDED (-1)MANDELIC ACID /IN RATS/, AS DID ACETOPHENONE & OMEGA-HYDROXYACETOPHENONE, THE STEREOSELECTIVE STEP MUST OCCUR DURING OXIDATION &/OR REDUCTION OF LATTER ... EITHER PATHWAY IS POSSIBLE, FOR ... PHENYLGLYOXAL & ... PHENYLETHYLENE GLYCOL ... YIELDED (-)MANDELIC ACID STEREOSELECTIVELY.
[The Chemical Society. Foreign Compound Metabolism in Mammals. Volume 5: A Review of the Literature Published during 1976 and 1977. London: The Chemical Society, 1979. 505]**PEER REVIEWED**

BENZOYLFORMIC ACID WAS BY-PRODUCT IN ALL ... EXPT /IN WHICH RATS WERE FED POSSIBLE INTERMEDIATES/. HOWEVER, WHEN THIS CMPD WAS FED, NO MANDELIC ACID WAS FORMED, & NEITHER WAS (-1)MANDELIC ACID CONVERTED INTO BENZOYLFORMIC ACID.
[The Chemical Society. Foreign Compound Metabolism in Mammals. Volume 5: A Review of the Literature Published during 1976 and 1977. London: The Chemical Society, 1979. 505]**PEER REVIEWED**

FEMALE ASSISTANTS USING MIXTURE OF XYLENES & ETHYLBENZENE AS SOLVENT IN HISTOLOGY LAB WERE EXAM. AVG AIR CONCN OF (M + P)-XYLENE & ETHYLBENZENE WAS BETWEEN 56-68 & 34-41 PPM. APPROX 1.1 TO 1.4% OF RETAINED ETHYLBENZENE WAS METABOLIZED TO 2-ETHYL-PHENOL.
[ANGERER J ET AL; INT ARCH OCCUP ENVIRON HEALTH 43 (2): 145 (1979)]**PEER REVIEWED**

IN 3 LAB TECHNICIANS OCCUPATIONALLY EXPOSED TO ETHYLBENZENE, THE URINARY METABOLITES WERE AMYGDALIC ACID, PHENYLGLYOXYLIC ACID & 2-ETHYLPHENOL; WITHIN 24 HR MORE THAN 90% OF METABOLITES HAD BEEN EXCRETED.
[HAGEMANN J ET AL; KREBSGEFAEHRDUNG ARBEITSPLATZ/ARBEITSMED KOLLOQ, BER JAHRESTAG DTSCH GES ARBEITSMED, 19TH: 421 (1979)]**PEER REVIEWED**

After ip administration of /4.45 g/ ethylbenzene /to rabbits/ ... o-, p-, and m-hydroxyacetophenone were

identified in urine. The above hydroxyacetophenones represented 0.11, 0.13, and 0.03% of the dose ... respectively.
[Kiese M, Lenk W; Xenobiotica 4: 337-43 (1974)]**PEER REVIEWED**

WHEN ABSORBED THROUGH SKIN, MANDELIC ACID WAS EXCRETED AT 4.6%, WHEREAS AFTER LUNG ABSORPTION MAJORITY OF ETHYLBENZENE WAS CONVERTED TO MANDELIC ACID & CONJUGATED WITH GLYCINE.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1343]**PEER REVIEWED**

After 2 volunteers were exposed to 65 ppm ethylbenzene for 3 hr, the metabolites of ethylbenzene in their urine, mandelic acid, hippuric acid (HA), and phenylglyoxylic (PhGA) were analyzed. The metabolites were excreted in the urine in the order mandelic acid > hippuric acid > phenylglyoxylic. The highest value of excretion was observed 6-10 hr after the beginning of exposure. Mandelic acid/phenylglyoxylic and hippuric/phenylglyoxylic mol ratios of total excretion in urine were 3.5 and 2.6 respectively.
[Yamasaki Y; Okayama Igakkai Zasshi 96 (5/6): 531-5 (1984)]**PEER REVIEWED**

The purpose of this study was to clarify whether the blood concentration of inhaled toluene, ethylbenzene, m-xylene, or mesitylene can change after the concomitant pulmonary absorption of **ethyl acetate. (**Adult female Sprague-Dawley rats were exposed in a 20 liter glass chamber under dynamic conditions for 2 hours to various concentrations of the aromatics without or in combination with different concentrations of **ethyl acetate (**0, 1000, or 4000 ppm) in air. Concentration ranges were as follows: toluene, 140-690 ppm; ethylbenzene, 120-650 ppm; m-xylene, 100-560 ppm; mesitylene, 120-720 ppm; and **ethyl acetate,** 1000 or 4000 ppm. The coexposures with **ethyl acetate** lowered the blood concentrations of other inhaled aromatics. This reduction was statistically significant following a 2 hour exposure to 230 ppm toluene in combination with 1000 ppm **ethyl acetate,** 650 ppm ethylbenzene with 1000 ppm **ethyl acetate,** and 100 ppm m-xylene with 4000 ppm **ethyl acetate.)** Similarly a significant reduction of the blood level of the aromatics by **ethyl acetate** coinhalation was also observed at higher exposure concentrations with toluene and m-xylene. A metabolic interaction such as enhanced disposition of the aromatics, may be responsible for these effects. However, it is possible that the solubility of the solvents could be altered by the presence of **ethyl acetate.** It was concluded that coexposures to concentrations in the order of the threshold limit values (100 ppm for these solvents) with 400 ppm **ethyl acetate** should not be followed by a dangerous change of the blood levels of the aromatics.
[Freundt KJ et al; Bull Environ Contam Toxicol 42 (4): 495-8 (1989)]**PEER REVIEWED**

Stereochemical considerations in the metabolism of ethylbenzene and styrene were investigated. Three alternative methods used to determine the enantiomeric composition of mandelic-acid in urine arising from exposure to styrene or ethylbenzene were described. Of the methods described, the direct gas chromatographic resolution of the enantiomers on a chiral stationary phase was the best approach. It was a simple analytical technique which avoids complex derivatization. An additional advantage was that it may be used as a gas liquid chromatography/mass spectrometry method and thus has advantages of sensitivity and specificity. F-19 nuclear magnetic resonance proved a useful alternative technique and

was invaluable if standards of the pure isomers were not available. The major advantage of the nuclear magnetic resonance approach was that absolute configuration of the compound could be elucidated. (In experimental studies, rats were administered ethylbenzene or styrene at 100 mg/kg by the stomach tube; urine was collected over 96 hours. Male volunteers were exposed to ethylbenzene vapor in an exposure chamber at 435 mg/cu m for 4 hours; urine samples were collected before, during and after exposure. The results indicate that whereas only the R-enantiomer of mardelic acid was excreted after ethylbenzene exposure, the mandelic acid from styrene was essentially racemic. In three workers exposed occupationally to styrene, R/S ratios of 1.16, 1.27 and 1.14 were found. A synthetic R/S mixture of mandelic acid has a R/S ratio of 1.03.)
[Drummond L et al; Xenobiotica 19 (2): 199-207 (1989)]**PEER REVIEWED**

The principal metabolites of ethyl benzene in the rabbit are hippuric acid and methylphenylcarbinyl glucosiduronic acid (the glucuronide of methylphenylcarbinol), which were excreted in roughly the same amounts and accounts for 60-70% of the administered dose. Minor metabolites were pharmaceutic acid (10-20%) and mandelic acid (2%).
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Volumes I,II, III. Cincinnati, OH: ACGIH, 1991. 583]**PEER REVIEWED**

Absorption, Distribution & Excretion:

ABSORPTION IS CHIEFLY BY INHALATION. A SMALL PROPORTION ... THAT GETS INTO THE BLOOD STREAM IS EXHALED UNCHANGED, BUT MOST OF IT /70%/ IS FOUND IN THE URINE AS METABOLITES BECAUSE OF OXIDATION OF THE SIDE CHAIN.
[Patty, F. (ed.). Industrial Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New York: Interscience Publishers, 1963. 1232]**PEER REVIEWED**

IT IS ABSORBED ... THROUGH SKIN AT LOW RATE. ... HAS BEEN DETECTED IN SUBCUTANEOUS ADIPOSE TISSUE SAMPLES OF WORKERS 3 DAYS AFTER LOW TO HIGH EXPOSURE TO STYRENE & RELATED RUBBER MFR COMPONENTS. ... HAS BEEN DETECTED IN CORD BLOOD SAMPLES, INDICATING ... TRANSPORT THROUGH PLACENTA.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1343]**PEER REVIEWED**

Traces of ethylbenzene have been detected in exhaled air. It also occurs in the gas phase of smoke condensate and has been detected at 3.1 to 4.5 ppb in urban air.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1342]**PEER REVIEWED**

THREE LAB TECHNICIANS EXPOSED TO 42 PPM & 1 TO 34 PPM HAD AVG STEADY STATE BLOOD LEVELS OF 0.72 + OR - 0.11 MG/L. 30 MIN AFTER EXPOSURE CONCN HAD DROPPED TO APPROX 0.5% OF ORIGINAL VALUES.
[HAGEMANN J ET AL, KREBSGEFAEHRDUNG ARBEITSPLATZ/ARBEITSMED KOLLOQ,

BER JAHRESTAG DTSCH GES ARBEITSMED 19TH: 421 (1979)]**PEER REVIEWED**

After exposure to 112-156 mg/l (aq) the skin absorption rate in humans (n= 14) was 0.11 to 0.21 mg/sq m/hr.
[Dutkiewicz T, Tyras H; Br J Ind Med 24 (4): 330-2 (1967)]**PEER REVIEWED**

When administered sc to 40 rats (2.5 ml, 1:1 v/v), ethylbenzene was detected in the blood within 2 hours, and the levels of ethylbenzene (10-15 ppm in blood) were maintained for at least 16 hours.
[USEPA; Ambient Water Quality Criteria Doc: Ethylbenzene p.C-6 (1980) EPA 440/5-80-048]**PEER REVIEWED**

After exposure of rats to atmospheres of 50, 300, or 600 ppm ethylbenzene 6 hr/day, 5 days/wk, for maximum of 16 wk, the concn of ethylbenzene in perirenal fat and the urinary excretion of 1-phenylethanol, omega-hydroxyacetophenone, mandelic acid, phenylglyoxylic acid, hippuric acid, and phenaceturic acid were measured at the 2nd, 5th, and 9th weeks. Excretion of metabolites into urine increased in a dose-related manner, but less than linearly. The level of exposure, but not the duration of exposure, markedly affected the pattern of the metabolites in the urine. The concn of ethylbenzene in perirenal fat was low at 50 ppm, high at 300 ppm and higher still at 600 ppm, but not in proportion to the increased dose.
[Engstroem K et al; Xenobiotica 15 (4): 281-6 (1985)]**PEER REVIEWED**

Percutaneous absorption of benzene, toluene, ethylbenzene, and aniline was investigated in male HRS/J hairless mice. Stainless steel skin depots containing 100 to 150 mg of solid sorbent were fixed to the backs of anesthetized mice and charged with about 5 ul of (14)C tagged test solution. Expired air samples were obtained until 4 hours after exposure, when mice were killed and samples for radioactivity were obtained from the skin depot, the skin under the depot, a wiping of the skin under the depot, the carcass, feces, urine, and cage washings. Physical constants were determined for each test compound, including octanol/water partition coefficient, solubility, vapor pressure, melting and boiling points, and absorption and evaporation rates. Solvent recovery exceeded 90% in all mice with highest recovery in the skin depot. Average administered doses were 3.94 mg benzene, of which 0.99% was absorbed; 3.89 mg toluene (2.31% absorbed), 4.10 mg ethylbenzene (3.61% absorbed), and 4.68 mg aniline (4.76% absorbed). Excretion rate in expired air was fastest during the first 15 minutes of exposure except in mice treated with toluene or ethylbenzene, which demonstrated maximal excretion rate during the second 15 minutes after exposure. A two compartment model was suggested by the initial rapid and subsequent gradual decay of expired breath excretion. Vapor pressure and boiling point were significantly correlated with the applied radioactive dose absorbed. Absorption rates were found to be 56, 49, 37, and 2.3 ug per square centimeter per minute for benzene, toluene, ethylbenzene, and aniline, respectively.
[Susten AS et al; J Appl Toxicol 10 (3): 217-25 (1990)]**PEER REVIEWED**

Mechanism of Action:

The effect of styrene, toluene, ethylbenzene, alpha-methylstyrene, and butylbenzene on oxidative phosphorylation was studied using rat liver mitochondrial preparations. Rat liver mitochondria were prepared from male white Wistar rats and assessed for respiration rate, oxygen uptake, glutamate oxidation, succinate oxidation, ATPase activity, and proton permeability in the presence and absence of the alkyl benzene derivatives. Inclusion of the alkyl benzene derivatives in the incubation medium

produced an initial acceleration of oxygen consumption followed by an inhibition of glutamate oxidation, and the stimulatory effect paralleled the aliphatic chain length. Glutamate oxidation was also inhibited by styrene, ethylbenzene, and alpha-methylstyrene but not by butylbenzene or toluene in 2,4-dinitrophenol uncoupled mitochondria. Styrene and the aliphatic benzene derivative stimulated succinate oxidation in rat liver mitochondria without effect on 2,4-dinitrophenol stimulated succinate oxidation. Similar stimulatory effects on ATPase activity were observed with maximal stimulation occurring at the same relative concentrations producing maximal succinate oxidation. ATPase stimulation required magnesium, was oligomycin sensitive, and showed an inverse relation to the hydrophobicity of the compounds tested. The inclusion of styrene in the incubation medium markedly increased the rate of passive entry of protons into rat liver mitochondria in a manner comparable to 2,4-dinitrophenol. It was concluded that styrene and other monosubstituted benzene derivatives act as mitochondrial uncoupling agents.
[Mickiewicz W, Rzeczycki W; Biochem Pharmacol 37 (23): 4439-44 (1988)]**PEER REVIEWED**

Effect of monocyclic aromatic hydrocarbons, their metabolites, and their structure on brain dopamine was studied. Adult male New Zealand rabbits were exposed to 750 ppm toluene, styrene, ethylbenzene, vinyltoluene, 7-methylstyrene, xylenes, and fresh air. Six groups of eight rabbits received 4 mM/kg ip for 3 days of hippuric acid, mandelic acid, methylhippuric acid, phenylglyoxylic acid, or 7-methylmandelic acid. Animals were killed 12 hours after inhalation exposure or 24 hours after the last dose of acid. The hypothalamus, striatum, hippocampus, tuberoinfundibular area, and part of the brain cortex were treated with 0.2 molar perchloric acid, homogenized, desorbed on alumina, and centrifuged. Supernatant was filtered and used to measure homovanillic acid. Styrene induced a marked dopamine depletion and a significant increase in homovanillic acid concentration. Ethylbenzene and vinyltoluene produced a smaller, but statistically significant effect. Toluene, xylenes, and 7-methylstyrene were ineffective. Phenylglyoxylic acid caused a decrease in dopamine levels and a consistent rise in homovanillic acid in striatal and tuberoinfundibular regions. Mandelic acid elicited the same effect, but to a lesser degree. 7-Methylmandelic, methylhippuric, and hippuric acids evoked no response. Neither solvents nor their metabolites affected norepinephrine contents of brain areas in which this neurotransmitter reaches high concentrations. It was concluded that the results indicate that the changes in brain dopamine depend on metabolic interferences of some metabolites of aromatic solvents with dopamine catabolism. Only metabolites whose side chain may be transformed into a alpha-keto acid caused dopamine depletion.
[Romanelli A et al; J Appl Toxicol 6 (6): 431-5 (1986)]**PEER REVIEWED**

The effect of organic solvents on the CNS was discussed. The similarity of effects of different solvents is believed to be due to the formation of tetrahydroisoquinolines by nonenzymatic condensation of dopamine with metabolites of organic solvents having a reactive carbonyl group. The suspected metabolites are phenylglyoxylic- acid that is formed by metabolism of ethylbenzene, styrene, vinyltoluene; trichloroacetaldehyde, which derives from trichloroethylene, tetrachloroethylene; and trichloroethane; glyoxylic acid that is synthesized from ethyleneglycol and ethyleneglycolmonomethyl ether; formaldehyde that is metabolized from methanol; and acetaldehyde that is transformed from ethanol. The tuberoinfundibular dopaminergic system may represent a target for metabolites dissolved in the blood stream. The suggested mechanism implies a selective vulnerability of pituitary functions. The impairment of tuberoinfundibular activity may explain most of the behavioral changes observed with styrene and perhaps with other similar solvents. It appears that the majority of pathways that are affected in the hypothalamic control of gonadotropins in primates are adrenergic and dopaminergic. Occupational

exposure to neurotoxins may cause repeated reversible CNS effects which are difficult to distinguish from the chronic effects. In workers exposed to styrene a relationship between recent exposure and measurable effects on CNS has been observed and prolonged exposure has failed to induce tolerance. It was concluded that although no excessive risk for Alzheimer disease and presenile dementia has been found, there is no indication that exposure to solvents does not cause irreversible or slowly reversible cognitive or neuropsychological impairment.
[Mutti A, Franchini I; Br J Ind Med 44 (11): 721-3 (1987)]**PEER REVIEWED**

Efforts were made to clarify the molecular basis of styrene toxicity on the dopaminergic systems and to evaluate whether the same mechanism was common to other solvents. Groups of male New Zealand rabbits were exposed to 750 ppm toluene, xylene, styrene, ethylbenzene, vinyltoluene, 7-methyl-styrene, or fresh air (control group). A significant depletion in both striatal and tubero infundibular dopamine was caused styrene, ethylbenzene, and vinyltoluene. Methylation of the aromatic ring of styrene did not change its activity, whereas methylation of the side chain drastically reduced its effect on dopamine. Treatments carried out with the main metabolites of aromatic solvents indicated that acidic metabolites of some solvents cause striatal and tubero infundibular dopamine depletion. Present data suggested a chemical reaction between dopamine and some acidic metabolites. The active metabolites have an alpha-keto acid as the side chain or as a part of their molecule. These keto acids condense nonenzymatically with dopamine in both experimental models and in occupational exposed workers as evidenced by the direct measurements of dopamine in the brain. According to the authors, such a mechanism may account for neurobehavioral effects resulting from solvent exposure such as mood changes, or impaired attention spans and decreasing psychomotor performance factors.
[Mutti A et al; Toxicol 49 (1, part 1): 77-82 (1988)]**PEER REVIEWED**

Interactions:

IN LAB ASSISTANTS USING XYLENES & ETHYLBENZENE, 2,4-DIMETHYLPHENOL, METAB OF M-XYLENE COULD NOT BE DETECTED. COMPETITIVE REACTION BETWEEN XYLENES & ETHYLBENZENE PREVENTED M-XYLENE FROM OXIDATION. ...
[ANGERER J ET AL; INT ARCH OCCUP ENVIRON HEALTH 43 (2): 145 (1979)]**PEER REVIEWED**

Pharmacology:

Interactions:

IN LAB ASSISTANTS USING XYLENES & ETHYLBENZENE, 2,4-DIMETHYLPHENOL, METAB OF M-XYLENE COULD NOT BE DETECTED. COMPETITIVE REACTION BETWEEN XYLENES & ETHYLBENZENE PREVENTED M-XYLENE FROM OXIDATION. ...
[ANGERER J ET AL; INT ARCH OCCUP ENVIRON HEALTH 43 (2): 145 (1979)]**PEER REVIEWED**

Environmental Fate & Exposure:

Environmental Fate/Exposure Summary:

Ethylbenzene's production and use as an intermediate for the production of styrene, its presence in

automotive and aviation fuels, and its presence in crude oil may result in its release to the environment through various waste streams. If released to air, a vapor pressure of 9.6 mm Hg at 25 deg C indicates ethylbenzene will exist solely as a vapor in the ambient atmosphere. Vapor-phase ethylbenzene will be degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals; the half-life for this reaction in air is estimated to be 55 hr. If released to soil, ethylbenzene is expected to have moderate mobility based upon an estimated Koc of 520. Volatilization from moist soil surfaces is expected to be an important fate process based upon a Henry's Law constant of 7.88X10-3 atm-cu m/mole. Ethylbenzene may volatilize from dry soil surfaces based upon its vapor pressure. Biodegradation in soil takes place via nitrate-reducing processes. If released into water, ethylbenzene may adsorb to suspended solids and sediment in water based upon the estimated Koc. Biodegradation in a gasoline contaminated aquifer ranged from 10-16 days under aerobic conditions. Ethylbenzene was degraded in 8 days in groundwater and 10 days in seawater as a component of gas oil. Volatilization from water surfaces is expected to be an important fate process based upon this compound's Henry's Law constant. Estimated volatilization half-lives for a model river and model lake are 1.1 and 99 hrs, respectively. Measured BCFs of 0.67 to 15 suggest the potential for bioconcentration in aquatic organisms is low. Hydrolysis is not expected to occur due to the lack of hydrolyzable functional groups. Occupational exposure to ethylbenzene may occur through inhalation at municipal waste composting facilities and via inhalation and dermal contact with this compound at workplaces where ethylbenzene is produced or used. The general population may be exposed to ethylbenzene via inhalation of ambient air, drinking and eating contaminated foods and water, and by handling gasoline. Ethylbenzene is likely to be detected in groundwater. (SRC)
PEER REVIEWED

Probable Routes of Human Exposure:

NIOSH (NOES Survey 1981-1983) has statistically estimated that 80,726 workers (21,785 of these are female) are potentially exposed to ethylbenzene in the US(1). Occupational exposure to ethylbenzene may occur via inhalation at municipal waste composting facilities where the air concn was found to be 78,000-178,000 ug/cu m(2),and through inhalation and dermal contact with this compound at worplaces where ethylbenzene is produced or used(SRC). The general population may be exposed to ethylbenzene via inhalation of ambient air, ingestion of foods and fish, and drinking contaminated water, and dermal contact with this compound and other products such as gasoline which contains ethylbenzene(SRC).
[(1) NIOSH; National Occupational Exposure Survey (NOES) (1983) (2) Eitzer BD; Environ Sci Technol 29: 896-902 (1995)]**PEER REVIEWED**

Body Burden:

Ethylbenzene was detected, not quantified, in 8 of 8 samples of mother's milk from 4 US urban areas(1). 16.5% of 387 expired air samples taken from 54 normal, healthy, urban volunteers were positive for ethylbenzene concn with an avg of 1.8 ng/l expired air(2). Whole blood samples from 250 subjects ranged in ethylbenzene concns from not detected to 59 ppb, with an avg of 1.0 ppb(3).
[(1) Pellizzari ED et al; Bull Environ Contam Toxicol 28: 322-8 (1982) (2) Krotoszynski BK et al; J Anal Toxicol 3: 225-34 (1979) (3) Antoine SR et al; Bull Environ Contam Toxicol 36: 364-71 (1986)]**PEER REVIEWED**

Average Daily Intake:

AIR INTAKE: (assume air concn of 0.2-2.7 ppb)(2-6); 17-235 ug; WATER INTAKE: (assume water concn of 0-4 ppb(1)) 0-8 ug; FOOD INTAKE: insufficient data(SRC).
[(1) Konasewich D et al; Status Report on Organic and Heavy Metal Contaminants in the Lake Erie, Michigan, Huron and Superior Basins. Great Lakes Quality Review Board (1978) (2) Arnts RR, Meeks SA; Biogenic Hydrocarbon Contribution to the Ambient Air of Selected Areas p. 31 USEPA-600/3-80-023 (1980) (3) Atshuller AP et al; Environ Sci Technol 5: 1009-16 (1981) (4) Lonneman WA et al; Environ Sci Technol 2: 1017-20 (1968) (5) Singh HB et al; Atmos Environ 15: 601-12 (1981) (6) Singh HB et al; Atmospheric Measurements of Selected Toxic Organic Chemicals USEPA-600/3-80-072 (1980)]**PEER REVIEWED**

Natural Pollution Sources:

Ethylbenzene is a product of biomass combustion(1), and a component of crude oil(2).
[(1) Graedel TE; Atmospheric Chemical Compounds. New York NY Academic Press (1986) (2) Nunes P, Benville PE JR; Bull Environ Contam Toxicol 21: 71-24 (1979)]**PEER REVIEWED**

Artificial Pollution Sources:

Ethylbenzene is present at 0.02 wt% in coke-oven tars.
[Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984.,p. V22 572 (1983)]**PEER REVIEWED**

Ethylbenzene's production and use as an intermediate for the manufacture of styrene and use as a resin solvent(1), intermediate for the production of diethylbenzene and acetophenone(2), and its use as a component of automotive and aviation fuels(3) may result in its release to the environment through various waste streams.
[(1) Budavari S, ed; The Merck Index. 12th ed. Whitehouse Station, NJ: Merck and Co., Inc. p. 643 (1996) (2) Coty RR et al; Ullmann's Encycl Indust Chem. 5th ed. Deerfield Beach, FL: VCH Pub A 10: 35-43 (1985) (3) Clayton GB, Clayton FE; Patty's Industrial Hygiene and Toxicology. 2B: Toxicology. 4th ed. NY, NY: John Wiley & Sons Inc 2B: 1342 (1994)]**PEER REVIEWED**

Environmental Fate:

TERRESTRIAL FATE: Based on a classification scheme(1), an estimated Koc value of 520(SRC), determined from a structure estimation method(2), indicates that ethylbenzene is expected to have moderate mobility in soil(SRC). Volatilization of ethylbenzene from moist soil surfaces is expected to be an important fate process(SRC) given a Henry's Law constant of 7.88X10-3 atm-cu m/mole(3). The potential for volatilization of ethylbenzene from dry soil surfaces may exist(SRC) based upon a vapor pressure of 9.6 mm Hg(4). Ethylbenzene was completely degraded in microcosms inoculated with the sediment material from a refinery pond or activated sludge from the refinery treatment facility under nitrate-reducing conditions(5). At Sleeping Bear Dunes National Lakeshore in Michigan, ethylbenzene was degraded at slow rates via anaerobic degradation under ambient subsurface conditions using ferric

iron, sulfate and/or carbon dioxide as the terminal electron acceptors(6).
[(1) Swann RL et al; Res Rev 85: 17-28 (1983) (2) Meylan WM et al; Environ Sci Technol 26: 1560-67 (1992) (3) Sanemasa I et al; Bull Chem Soc Japan 55: 1054-62 (1982) (4) Daubert TE et al; Physical and Thermodynamic Properties of Pure Chemicals. NY, NY: Hemisphere Pub Corp (1989) (5) Ball HA et al; pp. 458-63 in In-Situ Bioreclamation. Hinchee RE, Olfenbuttel RF, eds. Boston, MA: Butterworth-Heinemann (1991) (6) Borden RC et al; Anaerobic biodegradation of BTEX in aquifer material. USEPA/600/S-97/003 pp. 9 (1997)]**PEER REVIEWED**

AQUATIC FATE: Based on a classification scheme(1), an estimated Koc value of 520(SRC), determined from an estimation method(2), indicates that ethylbenzene may adsorb to suspended solids and sediment(SRC). Volatilization from water surfaces is expected(3) based upon a Henry's Law constant of 7.88X10-3 atm-cu m/mole(4). Using this Henry's Law constant and an estimation method(3), volatilization half-lives for a model river and model lake are 1.1 and 99 hr, respectively(SRC). According to a classification scheme(5), an experimental log BCF of 1.19(7), which corresponds to a BCF of 15, suggests the potential for bioconcentration in aquatic organisms is low. In a shallow coastal plain aquifer contaminated with gasoline and diesel fuel in rural Sampson County in North Carolina, ethylbenzene was degraded in aerobic conditions within 10-16 days and in conditions of low initial oxygen, it was rapidly degraded in 21 days until the available oxygen was depleted(8). As a component of gas oil, ethylbenzene is completely degraded in groundwater in 8 days(9) and seawater in 10 days(10). In a mesocosm experiment using simulated Narragansett Bay conditions, complete biodegradation occurred in approximately 2 days after a 2 week lag in spring and a 2 day lag in summer(11).
[(1) Swann RL et al; Res Rev 85: 17-28 (1983) (2) Meylan WM et al; Environ Sci Technol 26: 1560-67 (1992) (3) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington, DC: Amer Chem Soc pp. 4-9, 15-1 to 15-29 (1990) (4) Sanemasa I et al; Bull Chem Soc Japan 55: 1054-62 (1982) (5) France C et al; Chemosphere 29: 1501-14 (1994) (6) Hansch C et al; Exploring QSAR. Hydrophobic, Electronic, and Steric Constants. ACS Prof Ref Book. Heller SR, consult. ed., Washington, DC: Amer Chem Soc p. 43 (1995) (7) Park JH, Lee HJ; Chemosphere 26: 1905-16 (1993) (8) Borden RC et al; Water Resour Res 33: 1105-15 (1996) (9) Kappeler T, Wuhrmann K; Water Res 12: 327-33 (1978) (10) Van der Linden AC; Dev Biodegrad Hydrocarbons 1: 165-200 (1978) (11) Wakeham SG et al; Environ Sci Technol 17: 611-7 (1983)]**PEER REVIEWED**

ATMOSPHERIC FATE: According to a model of gas/particle partitioning of semivolatile organic compounds in the atmosphere(1), ethylbenzene, which has a vapor pressure of 9.6 mm Hg at 25 deg C(2), is expected to exist solely as a vapor. Vapor-phase ethylbenzene is degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals(SRC); the half-life for this reaction in air is 55 hr(SRC), calculated from its rate constant of 7.1X10-12 cu cm/molecule-sec at 25 deg C(3).
[(1) Bidleman TF; Environ Sci Technol 22: 361-367 (1988) (2) Daubert TE et al; Physical & Thermodynamic Properties of Pure Chemicals NY, NY: Hemisphere Pub Corp (1989) (3) Atkinson R; J Phys Chem Ref Data Monograph No. 2 p. 48 (1994)]**PEER REVIEWED**

Environmental Biodegradation:

After a period of inocula adaptation, ethylbenzene is biodegraded fairly rapidly by sewage or activated sludge inoculua(1-3,9). As a component of gas oil, it is completely degraded in groundwater in 8 days(4) and seawater in 10 days(5). In a mesocosm experiment using simulated Narragansett Bay conditions, complete biodegradation occurred in approximately 2 days after a 2 week lag in spring and a 2 day lag in summer(6). Part of the attenuation in concn from a leaky gasoline storage tank in the chalk aquifer in England has been attributed to biodegradation(7). No degradation was observed in an anaerobic reactor even after 110 days acclimation(8) or at low concentrations in a batch reactor in 11 weeks under denitrifying conditions(10). Percent removal in an anaerobic, continuous-flow, laboratory bioflim column was 7% after a 2 day detention time(11); 99% removal was observed in a similar aerobic column following a 20 min detention time(11).
[(1) Slave T et al; Rev Chim 25: 666-70 (1974) (2) Tabak HH et al; J Water Pollut Control Fed 53: 1503-18 (1981) (3) Malaney GW, McKinney RE; Water Sewage Works 113: 302-9 (1966) (4) Kappeler T, Wuhrmann K; Water Res 12: 327-33 (1978) (5) Van der Linden AC; Dev Biodegrad Hydrocarbons 1: 165-200 (1978) (6) Wakeham SG et al; Environ Sci Technol 17: 611-7 (1983) (7) Tester DJ, Harker RJ; Water Pollut Control 80: 614-31 (1981) (8) Chou WL et al; Biotechnol Bioeng Symp 8: 391-414 (1979) (9) USEPA; Treatability Manual p 1.9.8-1 to 1.9.8-5 USEPA 600/2-82-001a (1981) (10) Bouwer EJ, McCarty PL; Appl Environ Microbiol 45: 1295-99 (1983) (11) Bouwer EJ, McCarthy PL; Ground Water 22: 433-40 (1984)]**PEER REVIEWED**

AEROBIC: A study was conducted using underground storage tanks containing gasoline and diesel fuel that contaminated a shallow coastal plain aquifer in rural Sampson County in North Carolina. Ethylbenzene was degraded in aerobic conditions within 10-16 days and in conditions of low initial oxygen, it was rapidly degraded in 21 days until the available oxygen was depleted(1). A combined culture experiment of Mycobacterium vaccae and Rhodococcus sp. strain R-22 showed M. vaccae alone and M. vaccae and R-22 together can oxidize ethylbenzene to 4-ethylphenol which is then degraded to 50 ppm within 72 hr(2).
[(1) Borden RC et al; Water Resour Res 33: 1105-15 (1996) (2) Fairlee JR et al; J Microbiol 43: 841-6 (1997)]**PEER REVIEWED**

ANAEROBIC: Anaerobic ethylbenzene transformation in Seal Beach Naval Weapons Station sediments in Southern California appeared to be strictly associated with nitrate-reducing processes(1). Ethylbenzene was completely degraded in microcosms inoculated with the sediment material from a refinery pond or activated sludge from the refinery treatment facility under nitrate-reducing conditions(2). At Sleeping Bear Dunes National Lakeshore in Michigan, ethylbenzene was degraded at slow rates via anaerobic degradation under ambient subsurface conditions using ferric iron, sulfate and/or carbon dioxide as the terminal electron acceptors(3).
[(1) Ball HA, Reinhard M; Environ Toxicol Chem 15: 114-22 (1996) (2) Ball HA et al; pp. 458-63 in In-Situ Bioreclamation. Hinchee RE, Olfenbuttel RF, eds. Boston, MA: Butterworth-Heinemann (1991) (3) Borden RC et al; Anaerobic biodegradation of BTEX in aquifer material. USEPA/600/S-97/003 pp. 9 (1997)]**PEER REVIEWED**

Environmental Abiotic Degradation:

The rate constant for the vapor-phase reaction of ethylbenzene with photochemically-produced hydroxyl radicals is 7.1X10-12 cu cm/molecule-sec at 298 K(1) which corresponds to an atmospheric half-life of about 55 hr at an atmospheric concn of 5X10+5 hydroxyl radicals per cu cm. Ethylbenzene is not expected to undergo hydrolysis in the environment due to the lack of hydrolyzable functional groups(2). Ethylbenzene photolysis occurs via photooxidation hydrogen abstraction from the alkyl group by photooxydatively formed hydroxyl radical which results in the formation of acetophenone, and eventually benzaldehyde with 2-butanedial, 4-oxo-2-hexenal, and 2-ethyl-2-butenedial being suggested as further end products(3).
[(1) Atkinson R; J Phys Chem Ref Data Monograph No. 2 p. 48 (1994) (2) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington, DC: Amer Chem Soc pp. 7-4, 7-5 (1990) (3) Forstner HJL et al; Environ Sci Technol 31: 1345-58 (1997)]**PEER REVIEWED**

Environmental Bioconcentration:

Experimental data on the bioconcentration of ethylbenzene include a log BCF of 1.9 in goldfish(2) and a log BCF of 0.67 for clams exposed to the water-soluble fraction of crude oil(1). Experimentally, a log BCF of 1.19 has also been reported(4) which corresponds to a BCF of 15. According to a classification scheme(3), these BCFs suggest the potential for bioconcentration in aquatic organisms is low.
[(1) Nunes P, Benville PE Jr; Bull Environ Contam Toxicol 21: 719-24 (1979) (2) Ogata M et al; Bull Environ Contam Toxicol 33: 561-7 (1984) (3) Franke C et al; Chemosphere 29: 1501-14 (1994) (4) Park JH, Lee HJ; Chemosphere 26: 1905-16 (1993)]**PEER REVIEWED**

Soil Adsorption/Mobility:

Using a structure estimation method based on molecular connectivity indices(1), the Koc for ethylbenzene can be estimated to be 520(SRC). According to a classification scheme(2), this estimated Koc value suggests that ethylbenzene is expected to have low mobility in soil.
[(1) Meylan WM et al; Environ Sci Technol 26: 1560-67 (1992) (2) Swann RL et al; Res Rev 85: 17-28 (1983)]**PEER REVIEWED**

Volatilization from Water/Soil:

The Henry's Law constant for ethylbenzene is 7.88X10-3 atm-cu m/mole(1). This Henry's Law constant indicates that ethylbenzene will volatilize from water surfaces(2). Based on this Henry's Law constant, the volatilization half-life from a model river (1 m deep, flowing 1 m/sec, wind velocity of 3 m/sec)(2) is estimated as 1.1 hr(SRC). The volatilization half-life from a model lake (1 m deep, flowing 0.05 m/sec, wind velocity of 0.5 m/sec)(2) is estimated as 99 hr(SRC). Ethylbenzene's Henry's Law constant(1) indicates that volatilization from moist soil surfaces may occur(SRC). The potential for volatilization of ethylbenzene from dry soil surfaces may exist(SRC) based upon a vapor pressure of 9.6 mm Hg(3).
[(1) Sanemasa I et al; Bull Chem Soc Jpn 55: 1054-62 (1982) (2) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington, DC: Amer Chem Soc pp. 15-1 to 15-29 (1990) (3) Daubert TE et al; Physical & Thermodynamic Properties of Pure Chemicals NY, NY: Hemisphere Pub Corp (1989)]**PEER REVIEWED**

Environmental Water Concentrations:

DRINKING WATER: In surveys of representative US municipal water supplies, ethylbenzene has been detected in most cases(1,2,4-8,10). Values for 3 New Orleans finished drinking waters ranged 1.6 to 2.3 ppb(6). Chicago Central Water Works on Lake Michigan measured 4 ppb(8). It has been found in the water supply for Evansville, IN on the Ohio River(7). 6 of 10 US cities were found to be positive(1,4). One US city had 1 of 4 samples pos with a 1 ppb avg, while another reported no positive samples(5). Tap water from bank infiltrated Rhine River water in the Netherlands measured 30 ppb in one study(3). Zurich, Switzerland tap water - detected not quantified(9). 1982 US groundwater supply survey, random samples of finished water supplies using groundwater as a source, 466 random samples, 0.6%, pos (0.5 ppb detection limit), 0.8 ppb median, 1.1 ppb max(10).
[(1) NAS; The Alkylbenzenes p III-13 Contract 68-01-4655 (1980) (2) Shackelford WM, Keith, LH; Frequency of Organic Compounds in Surface Waters USEPA 600/4-76-062 (1976) (3) Piet GJ, Morra CF; p 31-42 in Artificial Groundwater Recharge; Huisman L, Olsthorn TN, eds (1983) (4) Bedding ND et al; Sci Total Environ 25: 143-67 (1982) (5) Callahan MA et al; p 55-61 in 8th Natl Conf Munic Sludge Manage Proc (1979) (6) Keith, LH et al; p 329-73 in Identification and Analysis of Organic Pollutants in Water. Keith LH ed (1976) (7) Kleopfer RD, Fairless BJ; Environ Sci Technol 6: 1036-7 (1972) (8) Konasewich D et al; Status Report on Organic and Heavy Metal Contaminants in the Lakes Erie, Michigan, Huron and Superior Basins. Great Lakes Quality Review Board (1978) (9) Santodonato J et al; Investigation of selected potential environmental contaminants: styrene, ethylbenzene and related compounds 261 p USEPA 560/11-80-018 (1980) (10) Cotruvo JA; Sci Technol Environ 47: 7-26 (1985)]**PEER REVIEWED**

GROUNDWATER: A well in Ames, IA measured 15 ppb 50 yr after tar residues were buried at a nearby coal gas plant(5). Concns of 82-400 ppb were detected in two aquifers near the Hoe Creek underground coal gasification site in Wyoming, 15 mo after gasification was complete(2). In a US survey, 1970-76, it was detected but not quantified in well waters(1). In Jackson Township, NJ, drinking water wells measured 2000 ppb(4). Chalk aquifer in East Anglia, England - 210 m from petroleum storage - 0.15 ppb, 10 m distance - 1110 ppb, and 100-200 m - <250 ppb(3).
[(1) Shackelford WM, Keith, LH; Frequency of Organic Compounds Identified in Water USEPA 600/4-76-062 (1976) (2) Stuermer DH et al; Environ Sci Technol 16: 582-7 (1982) (3) Tester DH, Harker RJ; Water Pollut Control 80: 614-31 (1981) (4) Burmaster DE; Environ 24: 6-13, 33-6 (1982) (5) Santodonato J et al; Investigation of Selected Potential Environmental Contaminants: Styrene, Ethylbenzene and Related Compounds 261 p USEPA 560/11-80-018 (1980)]**PEER REVIEWED**

SURFACE WATER: Ethylbenzene has been detected but not quantified in a 1970-76 US survey(1,4). 14 heavily industrialized US river basins, 5 of 204 sites pos - 1-4 ppb; Chicago area and Illinois River Basin, 5 of 31 sites pos - 1-4 ppb(6). Two representative US cities, city A - 41% of 28 samples pos, 5.0 ppb avg, city B - 40% of 48 samples pos 3.2 ppb avg(2). Lower Tennessee River near Calvert City, KY reported 4.0 ppb(7). Lake Michigan, Chicago Sanitary and Ship Channel measured 1-2 ppb(3). River Glatt, Switzerland -detected, not quantified(5). USEPA STORET database, 1,101 data points, 10% pos, <5.0

ppb median(8).
[(1) Shackelford WM, Keith LH; Frequency of Organic Compounds Identified in Water USEPA 600/4-76-062 (1976) (2) Callahan MA et al; p 55-61 in 8th Natl Conf Munic Sludge Manage Proc (1979) (3) Konasewich D et al; Status Report on Organic and Heavy Metal Contaminants in the Lakes Erie, Michigan, Huron and Superior Basins. Great Lakes Quality Review Board (1978) (4) Bertsch W et al; J Chromatogr 112: 701-18 (1975) (5) Zuercher F, Giger W; Vom Wasser 47: 37-55 (1976) (6) Ewing BB et al; Monitoring to Detect Previously Unrecognized Pollutants in Surface Waters 75 p USEPA 560/6-77-015 (appendix USEPA 560/6-77-015a) (1977) (7) Goodley PG, Gordon M; Kentucky Acad Sci 37: 11-5 (1976) (8) Staples CA et al; Environ Toxicol Chem 4: 131-42 (1985)]**PEER REVIEWED**

SEAWATER: Ethylbenzene concns were found to be 30-50 ng/l in an estuary in Brazos, US; between <10-46.3 ng/l in UK; and 36.9 ng/l in Belgium(1). Ethylbenzene has been found in concns of 4.5-30 ng/l in Vineyard Sound; 0.4-4.5 ng/l in coastal and shelf sea water in the Gulf of Mexico; 5.5-22 ng/l in the coastal waters of Spain; 4.3-380 ng/l in Campeche Shelf; <10 ng/l in shelf and bay waters in UK; and 9.4-18.7 ng/l in Belgian Continental Shelf(1). Ethylbenzene mean concn of 21.94 ng/l was found in the South Northern sea up to 60 km offshore in the Scheldt Estuary(2). In the coastal waters off the western Gulf of Mexico at the mouth of the Brazos River, TX, ethylbenzene concns range between 0.004-0.5 ug/l(3). In the Gulf of Mexico in unpolluted areas ethylbenzene concn is 0.4 to 5 ppb(4,6), while an area of anthropogenic influence ranged from 5 to 15 ppb(6). Cape Cod, MA measured ethylbenzene at 22 ppb(5,7) with 11 ppb being avg(5). In the coastal waters of the Dutch Northern Sea, 108 samples ranged from not detected to 20 parts per trillion and averaged 4 parts per trillion(8).
[(1) Dewulf J, Vanlangenhove H; Water Res 31: 1825-38 (1997) (2) Dewulf JP et al; Environ Sci Technol 32: 903-11 (1998) (3) Neff JM, Sauer TC Jr; Environ Sci Res 52: 163-75 (1996)(4) Sauer TC Jr et al; Mar Chem 7: 1-16 (1978) (5) Gschwend PM et al; Environ Sci Technol 16: 31-8 (1982) (6) Sauer TC Jr; Org Geochem 3: 91-101 (1981) (7) Mantoura RFC; Environ Sci Technol 16: 38-45 (1982) (8) Van de Meent D et al; Water Sci Technol 18: 73-81 (1986)]**PEER REVIEWED**

RAIN WATER: West Los Angeles, CA - 9 parts/trillion(1). Concn (parts/trillion) dissolved in rain, Portland, OR, Feb-April 1984, 7 rain events, 100% pos, 6.9-72, 34 avg(2).
[(1) Kawamura K, Kaplan IR; Environ Sci Technol 17: 497-501 (1983) (2) Ligocki MP; Atmos Environ 19: 1609-17 (1985)]**PEER REVIEWED**

Effluent Concentrations:

Industries with mean raw wastewater concentrations >2000 ppb: gum and wood chemicals (11,000 ppb), pharmaceutical manufacturing (10,000 ppb), paint and ink formulation, and auto and other laundries(1). Effluents from representative water treatment plants in Southern California were variable <10 ppb at San Diego City to 130 ppb at Los Angeles Co (both measurements following primary treatment)(2); <10 ppb detected following secondary treatment(2). In a US city survey, 17% of 6 samples were positive, 6.0 ppb avg(3), Lake Michigan, North Side sewage treatment plant - 1 ppb(4). USEPA STORET database, 1,368 data points, 7.4% pos, <3.0 ppb median(5). MN municipal solid waste landfills, leachates, 6 sites, 100%

pos, 12-820 ppb, contaminated groundwater (by inorganic indices), 13 sites, 61.5% pos, 1.2-590 ppb, other groundwater (apparently not contaminated as indicated by inorganic indices), 7 sites, 14.3% pos, 9.4 ppb avg(6). 18.0 and 12.28 kilotons of ethylbenzene was emitted as part of gasoline exhaust emissions from motor vehicles in 1987 and 1990, respectively in UK(7).
[(1) USEPA; Treatability Manual p.I.9.8-3 USEPA 600/2-82-001a (1981) (2) Young DR; 1978 Ann Rep Southern Calif Coastal Water Res Proj p 103-12 (1978) (3) Callahan MA et al; p 55-61 in 8th Natl Conf Munic Sludge Manage Proc (1979) (4) Konasewich D et al; Status Report on Organic and Heavy Metal Contaminants in Lakes Erie, Michigan, Huron and Superior basins. Great Lakes Qual Board 373 p (1979) (5) Staples CA et al; Environ Toxicol Chem 4: 131-42 (1985) (6) Sabel GV, Clark TP; Waste Manag Res 2: 119-30 (1984) (7) Field, RA et al; Atmos Environ 26A: 2983-96 (1992)]**PEER REVIEWED**

Sediment/Soil Concentrations:

SOIL: Ethylbenzene concns found in three leachate samples taken from German hazardous waste sites where leachate samples A and B were both anaerobic and alkaline and leachate sample C was aerobic and slightly acidic, were 10, 3200, and 20,000 ug/l, respectively(1). SEDIMENTS: Sediments from the lower Tennessee River below Calvert City, KY measured 4.0 ppb for ethylbenzene(2). According to the USEPA STORET database, 350 data points were tested for ethylbenzene with 11% pos, 5.0 ppm median, dry weight(3).
[(1) Brack W et al; Environ Toxicol Chem 17: 1982-91 (1998) (2) Goodley PC, Gordon M; Kentucky Acad Sci 37: 11-5 (1976) (3) Staples CA et al; Environ Technol Chem 4: 131-42 (1985)]**PEER REVIEWED**

Atmospheric Concentrations:

SOURCE DOMINATED: The ethylbenzene concn measured 0.5-2.6 ppb in the Allegheny Mt. Tunnel, with concns directly corresponding to the number of vehicles passing through the tunnel(1). Emissions testing from motor vehicle traffic in a Los Angeles roadway tunnel showed concns of 143 mg/l of ethylbenzene(2). The Maastunnel in the Netherlands measured an avg ethylbenzene concn of 6 ppb(3). Concn (ppb) a rural motorway in UK, May-Aug 1983, 184 samples, not detected-1.14, 0.17 avg(4); Aug 1982, not detected-0.70, 0.25 avg(5). Ethylbenzene ambient air concns at 2 landfill sites in Ireland were found to have a min and max of 0.03 and 5.9, median of 0.8 ug/cu m (site with no leachate collection), and 0.03 and 47.6, median of 5.3 ug/cu m (site with leachate collection), respectively(6). Houston, TX 21 individuals in urban sites reported a range of 2.5 to 154.2 ppb(8). A natural gas facility in Rio Blanco County, CO measured 3.6 ppb, and a Texaco refinery in Tulsa, OK ranged from 4.7 to 7.9 ppb(7). England - car park - 115 ppb, motorway - 92 ppb(9), while 6 sites at Gatwick airport ranged from 0.46 to 1.8 ppb, 1.4 ppb avg(10). 181 samples of US source dominated areas - 0.63 ppb avg(11).
[(1) Hampton CV et al; Environ Sci Technol 17: 699-708 (1983) (2) Fraser MP et al; Environ Sci Technol 32: 2051-60 (1998) (3) Bos R et al; Sci Total Environ 7: 269-81 (1977) (4) Clark AI et al; Sci Total Environ 39: 265-79 (1984) (5) Clark AI et al; Environ Pollut (Series B) 7: 141-58 (1984) (6) James KJ, Stack MA; Chemosphere 34: 1713-21 (1997) (7) Arnts RR, Meeks SA; Biogenic Hydrocarbon Contribution to the Ambient Air of Selected Areas 31 p USEPA 600/3-80-023 (1980) (8)

Lonneman WA et al; Hydrocarbons in Houston air. USEPA 600/3-79-018 pp. 44 (1979) (9) Perry R, Twibell JD; Atmos Environ 7: 329-37 (1973) (10) Tsani-Bazaca E et al; Chemosphere 11: 11-23 (1982) (11) Brodzinsky R, Singh HB; Volatile Organic Chemicals in the Atmosphere: An Assessment of Available Data. SRI Contract 68-02-3452 pp. 198 (1982)]**PEER REVIEWED**

URBAN/SUBURBAN: Values for major western US cities ranged from 0.1 to 27.7 ppb(1,5,6,7,13), with the avg being 2.68 ppb(SRC). Representative centers in New Jersey had a range of 0.17 to 0.33 ppb avg, 107 of 110 samples pos(4). Ethylbenzene was detected but not quantified in another New Jersey study(11). It has been detected in 6 USSR cities, including Lenningrad as well as New York and Paris(8-10). The Hague, Netherlands - 5 ppb(2); Sidney Australia - 1.3 ppb(12); Japan - 0.2 ppb and Frankfurt-am-Main, Germany - 1 ppb(14). 3 sites in England away from traffic - 16.1 to 18.8 parts/trillion avg, 2 sites with heavy traffic 28.7 to 33.9 parts/trillion avg(3). 8.7 ppb measured in the atmosphere of Zurich, Switzerland(17). 669 samples from the US had a median concn of 1.2 ppb(15). 36 Chicago metropolitan area homes tested - 36% in outdoor air(16). Gas-phase concn (ng/cu m) during 7 rain events, Portland, OR, Feb-Apri 1984, 7 rain events 100% pos, 780-2800, 1300 avg(20). Concn (ppb), Exhibition Road, London, May-Aug 1983, 267 samples, 100% pos, 0.05-2.17, 0.78 avg(18); June-July 1982, 256 samples, not detected-3.3, 0.88 avg(19). US 1979-1984, 15 cities, 1-2 weeks of sampling/site, overall range, not detected-31.5 ppb; range of avg, 0.6-4-6 ppb, avg of avg, 1.9 ppb(21). Ethylbenzene outdoor air concns in Rio de Janeiro, Brazil ranged from 3.1-7.4 ug/cu m(22).
[(1) Arnts RR, Meeks SA; Biogenic Hydrocarbon Contribution to the Ambient Air of Selected Areas. pp. 31 USEPA 600/3-80-023 (1980) (2) Bos R et al; Sci Total Environ 7: 269-81 (1977) (3) Thornburn S, Colenutt BA; Int J Environ Stud 13: 265-71 (1979) (4) Harkov R et al; J Air Pollut Control Assoc 33: 1177-83 (1983) (5) Altshuller AP et al; Environ Sci Technol 5: 1009-16 (1971) (6) Lonneman WA et al; Environ Sci Technol 2: 1017-20 (1968) (7) Singh HB et al; Atmos Environ 15: 601-12 (1981) (8) Ioffe BV et al; Dokl Akad Nauk SSSR 243: 1186-9 (1978) (9) Ioffe BV et al; Environ Sci Technol 13: 864-8 (1979) (10) Ioffe BV et al; J Chromatogr 142: 787-95 (1977) (11) Lioy P et al; J Water Pollut Control Fed 33: 649-57 (1983) (12) Nelson PF, Quigley SM; Atmos Environ 17: 659-62 (1983) (13) Singh HB et al; Atmospheric Measurements of Selected Toxic Organic Chemicals. USEPA 600/3-80-072 (1980) (14) Santodonato J et al; Investigation of Selected Potential Environmental Contaminants; Styrene, Ethyl Benzene and Related Compounds. pp. 261 USEPA 560/11-80-018 (1980) (15) Brodzinsky R, Singh HB; Volatile Organic Chemicals in the Atmosphere: An Assessment of Available Data 198 p SRI Contract 68-02-3452 (1982) (16) Jarke FH et al; ASHRAE Trans 87: 153-66 (1981) (17) Grob K, Grob g; J Chromatogr 62: 1-13 (1971) (18) Clark AI et al; Sci Total Environ 39: 265-79 (1984) (19) Clark AI et al; Environ Pollut (Series B) 7: 141-58 (1984) (20) Ligocki MP et al; Atmos Environ 19: 1609-17 (1985) (21) Singh HB et al; Atmos Environ 19: 1911-9 (1985) (22) Brickus LSR et al; Environ Sci Technol 32: 3485-90 (1998)]**PEER REVIEWED**

RURAL/REMOTE: Concentration in air sampls from rural and remote areas in the continental US ranged between 0.5 to 2.2 ppb(1,6). Samples from the Jones State Forest north of Houston, TX ranged from 0.8 to 10.4 ppb(3). Air intake in fan rooms of the Allegheny Mt. tunnel measured 0.07 to 0.16 ppb(2). Air samples in England - 11.3 parts/trillion avg(4); the Netherlands - 0.8 ppb avg; and Belgium 0.01 to 15 ppb(5). Concn at rural site in the UK, May-Aug 1983, 204 samples, not detected-0.70, 0.14 ppb avg(7); July 1982, 175 samples, not detected-0.6, 0.12 ppb avg(8).
[(1) Arnts RR, Meeks SA; Biogenic Hydrocarbon Contribution to the Ambient Air of Selected Areas. USEPA 600/3-80-023 pp. 31 (1980) (2) Hampton CV et al; Environ Sci Technol 17: 699-708 (1983) (3) Seila RL; Non-Urban Hydrocarbon Concentrations in Ambient Air North of Houston, TX. USEPA 500/3-79-010 pp. 38 (1979) (4) Thornburn S, Colenutt BA; Int J Environ Stud 13: 265-71 (1979) (5) Termonia M; pp. 356-61 in Comm Eur Comm EUR7624 Phys Chem Behav Atmos Pollut (1982) (6) Brodzinsky R, Singh HB; Volatile Organic Chemicals in the Atmosphere: An Assessment of Available Data. SRI Contract 68-02-3452 pp. 198 (1982) (7) Clark AI et al; Sci Total Environ 39: 265-79 (1984) (8) Clark AI et al; Environ Pollut (Series B) 7: 141-58 (1984)]**PEER REVIEWED**

RURAL/REMOTE: Between May-Aug 1983, 204 samples of air were tested for ethylbenzene at a rural site in UK and it was found that the sample concn ranged between not detected to 0.70 ppb, with an avg of 0.14 ppb(1). In July 1982, 175 samples from rural UK ranged between not detected to 0.6 ppb, with an avg of 0.12 ppb(2).
[(1) Clark AI et al; Sci Total Environ 39: 265-79 (1984) (2) Clark AI et al; Environ Pollut (Series B) 7: 141-58 (1984)]**PEER REVIEWED**

INDOOR: Ethylbenzene indoor air concns in Rio de Janeiro, Brazil ranged from 9.3-13.1 ug/cu m. samples from 36 Chicago metropolitan area homes tested showed a 57% detection frequency in indoor air(2).
[(1) Brickus LSR et al; Environ Sci Technol 32: 3485-90 (1998) (2) Jarke FH et al; ASHRAE Trans 87: 153-66 (1981)]**PEER REVIEWED**

Food Survey Values:

Ethylbenzene concns in supermarket eggs packed in polystyrene, fresh unpacked eggs, and fresh eggs packed in polystyrene were found to be 28, 4, and 4 ng/g, respectively(1). Duck meat, duck fat, cantonese style roasted duck, and cantonese style roasted duck gravy had concns of 0.47, 2.55, 4.07, and 12.30 ppb ethylbenzene, respectively(2). Ethylbenzene was detected but not quantified in mountain Beaufort cheese(3). Ethylbenzene was detected in dried legumes such as beans with a 5 ppb avg concn, in split peas at 13 ppb, and in lentils at a 5 ppb concn(4).
[(1) Matiella JE, Hsieh TCKY; J Food Sci 56: 387-90 (1991) (2) Wu CM, Liou SE; J Agric Food Chem 40: 838-41 (1992) (3) Dumont JP, Adda J; J Agric Food Chem 26: 364-7 (1978) (4) Lovegren NV et al; J Agric Food Chem 27: 851-3 (1979)]**PEER REVIEWED**

Fish/Seafood Concentrations:

In 1982, bottomfish (sole and flounder species) from Commencement Bay and adjacent waterways in Tacoma, WA were found to have an avg concn of ethylbenzene of 0.01 ppm(1). 5 samples of oysters in

Lake Pontchartrain, LA, had an avg concn of 0.8 ppb(2).
[(1) Nicola RM; J Environ Health 49: 342-7 (1987) (2) Ferrario JB et al; Bull Environ Contam Toxicol 34: 246-55 (1985)]**PEER REVIEWED**

Milk Concentrations:

Ethylbenzene was detected, but not quantified, in 8 of 8 samples of mother's milk from 4 US urban areas(1).
[(1) Pellizzari ED et al; Bull Environ Contam Toxicol 28: 322-8 (1982)]**PEER REVIEWED**

Other Environmental Concentrations:

Detected in cigarette smoke(1).
[(1) NAS; The Alkylbenzenes USEPA Contract No. 68-01-4655 (1980)]**PEER REVIEWED**

Environmental Standards & Regulations:

Acceptable Daily Intakes:

Acceptable daily intake: 1.6 mg/day
[USEPA; Ambient Water Quality Criteria Doc: Ethylbenzene p.C-22 (1980) EPA 440/5-80-048]**PEER REVIEWED**

TSCA Requirements:

Pursuant to section 8(d) of TSCA, EPA promulgated a model Health and Safety Data Reporting Rule. The section 8(d) model rule requires manufacturers, importers, and processors of listed chemical substances and mixtures to submit to EPA copies and lists of unpublished health and safety studies. Ethylbenzene is included on this list.
[40 CFR 716.120 (7/1/99)]**PEER REVIEWED**

CERCLA Reportable Quantities:

Persons in charge of vessels or facilities are required to notify the National Response Center (NRC) immediately, when there is a release of this designated hazardous substance, in an amount equal to or greater than its reportable quantity of 1000 lb or 454 kg. The toll free number of the NRC is (800) 424-8802; In the Washington D.C. metropolitan area (202) 426-2675. The rule for determining when notification is required is stated in 40 CFR 302.4 (section IV. D.3.b).
[40 CFR 302.4 (7/1/99)]**PEER REVIEWED**

RCRA Requirements:

F003; When ethylbenzene is a spent solvent, it is classified as a hazardous waste from a nonspecific source (F003), as stated in 40 CFR 261.31, and must be managed according to State and/or Federal hazardous waste regulations.
[40 CFR 261.31 (7/1/99)]**PEER REVIEWED**

Atmospheric Standards:

This action promulgates standards of performance for equipment leaks of Volatile Organic Compounds (VOC) in the Synthetic Organic Chemical Manufacturing Industry (SOCMI). The intended effect of these standards is to require all newly constructed, modified, and reconstructed SOCMI process units to use the best demonstrated system of continuous emission reduction for equipment leaks of VOC, considering costs, non air quality health and environmental impact and energy requirements. Ethylbenzene is produced, as an intermediate or a final product, by process units covered under this subpart.
[40 CFR 60.489 (7/1/99)]**PEER REVIEWED**

Listed as a hazardous air pollutant (HAP) generally known or suspected to cause serious health problems. The Clean Air Act, as amended in 1990, directs EPA to set standards requiring major sources to sharply reduce routine emissions of toxic pollutants. EPA is required to establish and phase in specific performance based standards for all air emission sources that emit one or more of the listed pollutants. Ethylbenzene is included on this list.
[Clean Air Act as amended in 1990, Sect. 112 (b) (1) Public Law 101-549 Nov. 15, 1990]**PEER REVIEWED**

Clean Water Act Requirements:

Toxic pollutant designated pursuant to section 307(a)(1) of the Federal Water Pollution Control Act and is subject to effluent limitations.
[40 CFR 401.15 (7/1/99)] **QC REVIEWED**

Ethylbenzene is designated as a hazardous substance under section 311(b)(2)(A) of the Federal Water Pollution Control Act and further regulated by the Clean Water Act Amendments of 1977 and 1978. These regulations apply to discharges of this substance. This designation includes any isomers and hydrates, as well as any solutions and mixtures containing this substance.
[40 CFR 116.4 (7/1/99)] **QC REVIEWED**

For the protection of human health from the toxic properties of ethylbenzene ... the ambient water criterion is determined to be 1.4 mg/l.
[USEPA; Quality Criteria for Water 1986: Ethylbenzene (May 1,1986) EPA 440/5-86-001] **QC REVIEWED**

The maximum contaminant level (MCL) set forth by the National Revised Primary Drinking Water Regulations for the organic contaminant ethylbenzene in community and non-transient, non-community water systems is 0.7 mg/l.
[40 CFR 141.61 (7/1/99)] **QC REVIEWED**

Federal Drinking Water Standards:

EPA 700 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

Federal Drinking Water Guidelines:

EPA 700 ug/l

[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

State Drinking Water Guidelines:

(AZ) ARIZONA 680 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

(FL) FLORIDA 30 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

(ME) MAINE 700 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

(MN) MINNESOTA 700 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

Chemical/Physical Properties:

Molecular Formula:

C8-H10
PEER REVIEWED

Molecular Weight:

106.16
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 643]**PEER REVIEWED**

Color/Form:

Colorless liquid
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 1997. 461]**PEER REVIEWED**

Odor:

Aromatic odor
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 13th

ed. New York, NY: John Wiley & Sons, Inc. 1997. 461]**PEER REVIEWED**

Pungent odor
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1342]**PEER REVIEWED**

SWEET, GASOLINE-LIKE ODOR
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Boiling Point:

136.1 deg C
[Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 79th ed. Boca Raton, FL: CRC Press Inc., 1998-1999.,p. 3-47]**PEER REVIEWED**

Melting Point:

-94.9 deg C
[Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 79th ed. Boca Raton, FL: CRC Press Inc., 1998-1999.,p. 3-47]**PEER REVIEWED**

Critical Temperature & Pressure:

Critical temperature = 617.15 K; critical pressure = 3.6X10+6 Pa
[Daubert, T.E., R.P. Danner. Physical and Thermodynamic Properties of Pure Chemicals Data Compilation. Washington, D.C.: Taylor and Francis, 1989.]**PEER REVIEWED**

Density/Specific Gravity:

0.8670 @ 20 deg C/4 deg C
[Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 79th ed. Boca Raton, FL: CRC Press Inc., 1998-1999.,p. 3-47]**PEER REVIEWED**

Heat of Combustion:

-17,780 BTU/lb= -9877 cal/g= -413.5x10+5 J/kg
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Heat of Vaporization:

4.8X10+7 J/kmol @ 178.20 K
[Daubert, T.E., R.P. Danner. Physical and Thermodynamic Properties of Pure Chemicals Data Compilation. Washington, D.C.: Taylor and Francis, 1989.]**PEER REVIEWED**

Octanol/Water Partition Coefficient:

log Kow= 3.15
[Hansch, C., Leo, A., D. Hoekman. Exploring QSAR - Hydrophobic, Electronic, and Steric Constants. Washington, DC: American Chemical Society., 1995. 43]**PEER REVIEWED**

Solubilities:

SOL IN ALL PROPORTIONS IN ETHYL ALCOHOL AND ETHYL ETHER
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 2114]**PEER REVIEWED**

SOLUBILITY IN WATER @ 15 DEG C, 0.014 G/100 ML
[Patty, F. (ed.). Industrial Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New York: Interscience Publishers, 1963. 1223]**PEER REVIEWED**

Miscible with the usual organic solvents.
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 643]**PEER REVIEWED**

Soluble in alcohol, benzene, carbon tetrachloride, and ether.
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 1997. 461]**PEER REVIEWED**

Slight soluble in chloroform; miscible in ethanol and ethyl ether.
[Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 79th ed. Boca Raton, FL: CRC Press Inc., 1998-1999.,p. 3-47]**PEER REVIEWED**

In water, 169 mg/l @ 25 deg C
[Sanemasa I et al; Bull Chem Soc Japan 55: 1054-62 (1982)]**PEER REVIEWED**

Insol in ammonia; sol in SO2.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1522]**PEER REVIEWED**

Spectral Properties:

SADTLER REF NUMBER: 246 (IR, PRISM); 82 (IR, GRATING)
[Weast, R.C. (ed.). Handbook of Chemistry and Physics. 60th ed. Boca Raton, Florida: CRC Press Inc., 1979.,p. C-165]**PEER REVIEWED**

IR: 4779 (Coblentz Society Spectral Collection)
[Weast, R.C. and M.J. Astle. CRC Handbook of Data on Organic Compounds. Volumes I and II. Boca Raton, FL: CRC Press Inc. 1985.,p.

V1 613]**PEER REVIEWED**

UV: 97 (Sadtler Research Laboratories Spectral Collection)
[Weast, R.C. and M.J. Astle. CRC Handbook of Data on Organic Compounds. Volumes I and II. Boca Raton, FL: CRC Press Inc. 1985.,p. V1 613]**PEER REVIEWED**

NMR: 505 (Varian Associates NMR Spectra Catalogue)
[Weast, R.C. and M.J. Astle. CRC Handbook of Data on Organic Compounds. Volumes I and II. Boca Raton, FL: CRC Press Inc. 1985.,p. V1 613]**PEER REVIEWED**

MASS: 322 (Atlas of Mass Spectral Data, John Wiley & Sons, New York)
[Weast, R.C. and M.J. Astle. CRC Handbook of Data on Organic Compounds. Volumes I and II. Boca Raton, FL: CRC Press Inc. 1985.,p. V1 613]**PEER REVIEWED**

Index of refraction: 1.4959 at 20 deg C/D
[Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 79th ed. Boca Raton, FL: CRC Press Inc., 1998-1999.,p. 3-47]**PEER REVIEWED**

Surface Tension:

4.3 N/m @ 178.20 K
[Daubert, T.E., R.P. Danner. Physical and Thermodynamic Properties of Pure Chemicals Data Compilation. Washington, D.C.: Taylor and Francis, 1989.]**PEER REVIEWED**

Vapor Density:

3.66 (Air= 1)
[Sax, N.I. Dangerous Properties of Industrial Materials. Vol 1-3 7th ed. New York, NY: Van Nostrand Reinhold, 1989. 1601]**PEER REVIEWED**

Vapor Pressure:

9.6 mm Hg @ 25 deg C
[Daubert, T.E., R.P. Danner. Physical and Thermodynamic Properties of Pure Chemicals Data Compilation. Washington, D.C.: Taylor and Francis, 1989.]**PEER REVIEWED**

Relative Evaporation Rate:

IT EVAPORATES ABOUT 94 TIMES MORE SLOWLY THAN ETHER
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1342]**PEER REVIEWED**

Viscosity:

0.64 cP @ 25 deg C

[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 1997. 461]**PEER REVIEWED**

Other Chemical/Physical Properties:

DENSITY OF SATURATED VAPOR-AIR MIXTURE AT 760 MM HG (AIR= 1): 1.03 (26 DEG C); SPECIFIC DISPERSION: 174.6
[Patty, F. (ed.). Industrial Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New York: Interscience Publishers, 1963. 1223]**PEER REVIEWED**

CONVERSION FACTORS: 1 MG/L IS EQUIVALENT TO 230 PPM, 1 PPM IS EQUIVALENT TO 4.35 MG/CU M AT 25 DEG C, 760 MM HG
[Patty, F. (ed.). Industrial Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New York: Interscience Publishers, 1963. 1231]**PEER REVIEWED**

Specific heat: 0.41 cal/gal/K
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 1997. 461]**PEER REVIEWED**

Liquid-water interfacial tension: 35.48 dynes/cm= 0.03548 N/m @ 20 deg C
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Ratio of Specific Heats of Vapor (gas): 1.071
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Heats of transition, J/(mol.K): fusion 9.164; formation @ 25 deg C: -12.456; entropy of formation 255.2
[Kirk-Othmer Encyclopedia of Chemical Technology. 4th ed. Volumes 1: New York, NY. John Wiley and Sons, 1991-Present.,p. V5 833]**PEER REVIEWED**

Cricital density: 2.67 mmol/cu m; critical volume: 374.0 cu m/mol
[Kirk-Othmer Encyclopedia of Chemical Technology. 4th ed. Volumes 1: New York, NY. John Wiley and Sons, 1991-Present.,p. V25 833]**PEER REVIEWED**

Viscosity: 0.678 mPas (20 deg C)
[Environment Canada; Tech Info for Problem Spills: Ethylbenzene p.4 (1981)]**PEER REVIEWED**

Ionization potential: 8.76 eV
[Environment Canada; Tech Info for Problem Spills: Ethylbenzene p.4 (1981)]**PEER REVIEWED**

Flame speed: 0.35 m/s

[Environment Canada; Tech Info for Problem Spills: Ethylbenzene p.2 (1981)]**PEER REVIEWED**

Partition coefficients at 37 deg C for ethylbenzene into blood= 28.4; into oil= 3,790.
[Sato A, Nakajima T; Scand J Work Environ Health 13: 81-93 (1987)]**PEER REVIEWED**

Henry's Law constant= 7.88X10-3 atm-cu m/mol @ 25 deg C
[Sanemasa I et al; Bull Chem Soc Japan 55: 1054-62 (1982)]**PEER REVIEWED**

Hydroxyl radical rate constant= 7.10X10-12 cu m/molecule-sec @ 25 deg C
[Atkinson R; J Phys Chem Ref Data Monograph No. 2 p. 48 (1994)]**PEER REVIEWED**

Chemical Safety & Handling:

DOT Emergency Guidelines:

Fire or explosion: Highly flammable: Will be easily ignited by heat, sparks or flames. Vapors may form explosive mixtures with air. Vapors may travel to source of ignition and flash back. Most vapors are heavier than air. They will spread along ground and collect in low confined areas (sewers, basements, tanks). Vapor explosion hazard indoors, outdoors or in sewers. Some may polymerize (P) explosively when heated or involved in a fire. Runoff to sewer may create fire or explosion hazard. Containers may explode when heated. Many liquids are lighter than water.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

Health: May cause toxic effects if inhaled or absorbed through skin. Inhalation or contact with material may irritate or burn skin and eyes. Fire will produce irritating, corrosive and/or toxic gases. Vapors may cause dizziness or suffocation. Runoff from fire control or dilution water may cause pollution.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

Public safety: Call Emergency Response Telephone Number. ... Isolate spill or leak area immediately for at least 50 to lOO meters (160 to 330 feet) in all directions. Keep unauthorized personnel away. Stay upwind. Keep out of low areas. Ventilate closed spaces before entering.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S.

Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

Protective clothing: Wear positive pressure self-contained breathing apparatus (SCBA). Structural firefighters' protective clothing will only provide limited protection.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

Evacuation: Large spill: Consider initial downwind evacuation for at least 300 meters (1000 feet). Fire: If tank, rail car or tank truck is involved in a fire, isolate for 800 meters (1/2 mile) in all directions; also, consider initial evacuation for 800 meters (1/2 mile) in all directions.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

Fire: Caution: All these products have a very low flash point: Use of water spray when fighting fire may be inefficient. Small fires: Dry chemical, CO2, water spray or alcohol-resistant foam. Do not use dry chemical extinguishers to control fires involving nitromethane or nitroethane. Large fires: Water spray, fog or alcohol-resistant foam. Do not use straight streams. Move containers from fire area if you can do it without risk. Fire involving tanks or car/trailer loads: Fight fire from maximum distance or use unmanned hose holders or monitor nozzles. Cool containers with flooding quantities of water until well after fire is out. Withdraw immediately in case of rising sound from venting safety devices or discoloration of tank. Always stay away from the ends of tanks. For massive fire, use unmanned hose holders or monitor nozzles; if this is impossible, withdraw from area and let fire burn.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

Spill or leak: Eliminate all ignition sources (no smoking, flares, sparks or flames in immediate area). All equipment used when handling the product must be grounded. Do not touch or walk through spilled material. Stop leak if you can do it without risk. Prevent entry into waterways, sewers, basements or confined areas. A vapor suppressing foam may be used to reduce vapors. Absorb or cover with dry earth, sand or other non-combustible material and transfer to containers. Use clean non-sparking tools to collect absorbed material. Large spills: Dike far ahead of liquid spill for later disposal. Water spray may reduce vapor; but may not prevent ignition in closed spaces.
[U.S. Department of Transportation. 1996 North American Emergency

Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

First aid: Move victim to fresh air. Call emergency medical care. Apply artificial respiration if victim is not breathing. Administer oxygen if breathing is difficult. Remove and isolate contaminated clothing and shoes. In case of contact with substance, immediately flush skin or eyes with running water for at least 20 minutes. Wash skin with soap and water. Keep victim warm and quiet. Effects of exposure (inhalation, ingestion or skin contact) to substance may be delayed. Ensure that medical personnel are aware of the material(s) involved, and take precautions to protect themselves.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

Odor Threshold:

140 ppm /Purity not specified/
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

2-2.6 mg/cu m; detection: 0.4 mg/cu m /Purity not specified/
[Verschueren, K. Handbook of Environmental Data on Organic Chemicals. 3rd ed. New York, NY: Van Nostrand Reinhold Co., 1996. 944]**PEER REVIEWED**

Odor Low: 8.7 mg/cu m, Odor High: 870.0 mg/cu m
[Ruth JH; Am Ind Hyg Assoc J 47: A-142-51 (1986)]**PEER REVIEWED**

Skin, Eye and Respiratory Irritations:

... CHARACTERIZED ... AS MOST SEVERE IRRITANT OF THE BENZENE SERIES.
[American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices. 5th ed. Cincinnati, OH:American Conference of Governmental Industrial Hygienists, 1986. 244]**PEER REVIEWED**

A concn of 200 ppm causes eye irritation. A concn of 100 ppm for 8 hr caused irritative effects in a human.
[Cleland, J.G., G.L. Kingsbury. Multimedia Environmental Goals for Environmental Assessment. Volume 1. EPA-600/7-77-136a. Research Triangle Park, NC: EPA, Nov. 1977.,p. E-148]**PEER REVIEWED**

EXPOSURE TO CONCN OF 5000 PPM /24.6 MG/L/ ... CAUSES INTOLERABLE IRRITATION OF

EYES, MUCOUS MEMBRANES & NOSE.
[Patty, F. (ed.). Industrial Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New York: Interscience Publishers, 1963. 1232]**PEER REVIEWED**

HAZARD WARNING: ... exposure to 21.5 g/cu m (5000 ppm) ethylbenzene for a few seconds gives intolerable irritation of nose, eyes, and throat.
[Environmental Health Criteria 186: Ethylbenzene pp. 67 (1996) by the International Programme on Chemical Safety (IPCS) under the joint sponsorship of the United Nations Environment Programme, the International Labour Organisation and the World Health Organization.]**QC REVIEWED**

Fire Potential:

A very dangerous fire ... hazard when exposed to heat or flame ...
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1522]**PEER REVIEWED**

Electrical ignition hazard: May be ignited by static discharge.
[Environment Canada; Tech Info for Problem Spills: Ethylbenzene (Draft) p.4 (1982)]**PEER REVIEWED**

NFPA Hazard Classification:

Health: 2. 2= Materials that, on intense or continued (but not chronic) exposure, could cause temporary incapacitation or possible residual injury, including those requiring the use of respiratory protective equipment that has an independent air supply. These materials are hazardous to health, but areas may be entered freely if personnel are provided with full-face mask self-contained breathing apparatus that provides complete eye protection.
[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 325-48]**PEER REVIEWED**

Flammability: 3. 3= This degree includes Class IB and IC flammable liquids and materials that can be easily ignited under almost all normal temperature conditions. Water may be ineffective in controlling or extinguishing fires in such materials.
[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 325-48]**PEER REVIEWED**

Reactivity: 0. 0= This degree includes materials that are normally stable, even under fire exposure conditions, and that do not react with water. Normal fire fighting procedures may be used.
[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 325-48]**PEER REVIEWED**

Flammable Limits:

Lower flammable limit: 0.8% by volume; Upper flammable limit: 6.7% by volume
[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 325-48]**PEER REVIEWED**

Flash Point:

12.8 DEG C (55 DEG F) (CLOSED CUP)
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1304]**PEER REVIEWED**

Autoignition Temperature:

810 DEG F
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1522]**PEER REVIEWED**

Fire Fighting Procedures:

Approach fire from upwind to avoid hazardous vapors and toxic decomposition products. Use water spray, dry chemical, foam, or carbon dioxide. Use water spray to keep fire-exposed containers cool.
[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 49-65]**PEER REVIEWED**

If material on fire or involved in fire: Do not extinguish fire unless flow can be stopped or safely confined. Use water in flooding quantities as fog. Solid streams of water may spread fire. Cool all affected containers with flooding quantities of water. Apply water from as far a distance as possible. Use foam, carbon dioxide, or dry chemical.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 443]**PEER REVIEWED**

Toxic Combustion Products:

Irritating vapors are generated when heated.
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

The combustion products of ethylbenzene are water and carbon dioxide or carbon monoxide in limited oxygen atmospheres.
[Environment Canada; Tech Info for Problem Spills: Ethylbenzene (Draft) p.79 (1982)]**PEER REVIEWED**

Compounds identified in tars produced by the pyrolysis of ethylbenzene include the following suspected carcinogens: 1-benzanthracene, benzene, benzofluoranthene, 10,11-benzofluoranthene, 12-benzofluoranthene, 1-benzofluoranthene, 1-benzopyrene, 3,4-benzopyrene, chrysene, and

1,2:5,6-dibenzanthracene.
[NAS; The Alkylbenzenes p.99 (1981)]**PEER REVIEWED**

Firefighting Hazards:

Vapors are heavier than air and may travel to a source of ignition and flash back. Liquid floats on water and may travel to a source of ignition and spread fire.
[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 49-65]**PEER REVIEWED**

Explosive Limits & Potential:

Vapors form explosive mixtures with air.
[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 49-65]**PEER REVIEWED**

Lower explosive limit= 1.2%. Upper explosive limit= 6.8%.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1522]**PEER REVIEWED**

Hazardous Reactivities & Incompatibilities:

Incompatibilities: Strong oxidizers.
[Sittig, M. Handbook of Toxic and Hazardous Chemicals and Carcinogens, 1985. 2nd ed. Park Ridge, NJ: Noyes Data Corporation, 1985. 4122]**PEER REVIEWED**

... Can react vigorously with oxidizing materials.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1522]**PEER REVIEWED**

Strong oxidizers.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 132]**PEER REVIEWED**

Hazardous Decomposition:

When heated to decomposition it emits acrid smoke and irritating fumes.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1522]**PEER REVIEWED**

Immediately Dangerous to Life or Health:

800 ppm
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing

Office, 1997. 132]**PEER REVIEWED**

Protective Equipment & Clothing:

Wear full protective clothing and positive pressure self-contained breathing apparatus.
[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 49-65]**PEER REVIEWED**

Rubber overclothing (including gloves)
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Wear appropriate personal protective clothing to prevent skin contact.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 132]**PEER REVIEWED**

Wear appropriate eye protection to prevent eye contact.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 132]**PEER REVIEWED**

Recommendations for respirator selection. Max concn for use: 800 ppm. Respirator Class(es): Any chemical cartridge respirator with organic vapor cartridge(s). May require eye protection. Any air-purifying, full-facepiece respirator (gas mask) with a chin-style, front- or back-mounted organic vapor canister. Any powered, air-purifying respirator with organic vapor cartridge(s). May require eye protection. Any supplied-air respirator. May require eye protection. Any self-contained breathing apparatus with a full facepiece.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 132]**PEER REVIEWED**

Recommendations for respirator selection. Condition: Emergency or planned entry into unknown concn or IDLH conditions: Respirator Class(es): Any self-contained breathing apparatus that has a full facepiece and is operated in a pressure-demand or other positive-pressure mode. Any supplied-air respirator that has a full facepiece and is operated in a pressure-demand or other positive-pressure mode in combination with an auxiliary self-contained breathing apparatus operated in pressure-demand or other positive-pressure mode.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 132]**PEER REVIEWED**

Recommendations for respirator selection. Condition: Escape from suddenly occurring respiratory hazards: Respirator Class(es): Any air-purifying, full-facepiece respirator (gas mask) with a chin-style, front- or back-mounted organic vapor canister. Any appropriate escape-type, self-contained breathing apparatus.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing

Office, 1997. 132]**PEER REVIEWED**

Preventive Measures:

Contact lenses should not be worn when working with this chemical.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 132]**PEER REVIEWED**

SRP: The scientific literature for the use of contact lenses in industry is conflicting. The benefit or detrimental effects of wearing contact lenses depend not only upon the substance, but also on factors including the form of the substance, characteristics and duration of the exposure, the uses of other eye protection equipment, and the hygiene of the lenses. However, there may be individual substances whose irritating or corrosive properties are such that the wearing of contact lenses would be harmful to the eye. In those specific cases, contact lenses should not be worn. In any event, the usual eye protection equipment should be worn even when contact lenses are in place.
PEER REVIEWED

Employees should wash promptly when skin is wet or contaminated. Remove clothing immediately if wet or contaminated to avoid flammability hazard.
[Sittig, M. Handbook of Toxic and Hazardous Chemicals and Carcinogens, 1985. 2nd ed. Park Ridge, NJ: Noyes Data Corporation, 1985. 414]**PEER REVIEWED**

BEFORE WORKERS ARE ALLOWED TO ENTER A REACTION VESSEL ... THE VESSEL SHOULD BE PURGED AND WELL VENTILATED. PERSONAL PROTECTIVE EQUIPMENT SHOULD BE SUPPLIED ...
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 2114]**PEER REVIEWED**

... SUBSTITUTION OF LESS IRRITATING SUBSTANCES, ... REDESIGN OF OPERATIONS, ... PREVENT CONTACT, PROVISION OF A PHYSICAL BARRIER AGAINST CONTACT, PROPER WASHING FACILITIES, PROPER WORK CLOTHING AND STORAGE FACILITIES, PROTECTIVE CLOTHING, BARRIER CREAMS, AND MEDICAL CONTROL ...
[Sax, N.I. Dangerous Properties of Industrial Materials. 4th ed. New York: Van Nostrand Reinhold, 1975. 727]**PEER REVIEWED**

Personnel protection: Avoid breathing vapors. Keep upwind. ... Do not handle broken packages without protective equipment. Wash away any material which may have contacted the body with copious amounts of water or soap and water.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 443]**PEER REVIEWED**

COMBUSTION MAY BE IMPROVED BY MIXING WITH MORE FLAMMABLE LIQ. ... SHOULD NOT BE ALLOWED TO ENTER CONFINED SPACE, SUCH AS SEWER, BECAUSE OF POSSIBILITY OF EXPLOSION.
[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.).

NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) PublicationNo. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981. 2]**PEER REVIEWED**

If material not on fire and not involved in fire: Keep sparks, flames, and other sources of ignition away. Keep material out of water sources and sewers. Build dikes to contain flow as necessary. Attempt to stop leak if without hazard. Use water spray to knock-down vapors.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 443]**PEER REVIEWED**

The worker should immediately wash the skin when it becomes contaminated.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 132]**PEER REVIEWED**

Work clothing that becomes wet should be immediately removed due to its flammability hazard.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 132]**PEER REVIEWED**

Shipment Methods and Regulations:

No person may /transport,/ offer or accept a hazardous material for transportation in commerce unless that person is registered in conformance ... and the hazardous material is properly classed, described, packaged, marked, labeled, and in condition for shipment as required or authorized by ... /the hazardous materials regulations (49 CFR 171-177)./
[49 CFR 171.2 (7/1/99)]**PEER REVIEWED**

The International Air Transport Association (IATA) Dangerous Goods Regulations are published by the IATA Dangerous Goods Board pursuant to IATA Resolutions 618 and 619 and constitute a manual of industry carrier regulations to be followed by all IATA Member airlines when transporting hazardous materials.
[IATA. Dangerous Goods Regulations. 40th Ed. Montreal, Canada and Geneva, Switzerland: International Air Transport Association, Dangerous Goods Regulations, 1999. 149]**PEER REVIEWED**

The International Maritime Dangerous Goods Code lays down basic principles for transporting hazardous chemicals. Detailed recommendations for individual substances and a number of recommendations for good practice are included in the classes dealing with such substances. A general index of technical names has also been compiled. This index should always be consulted when attempting to locate the appropriate procedures to be used when shipping any substance or article.
[IMDG; International Maritime Dangerous Goods Code; International Maritime Organization p.3222 (1998)]**PEER REVIEWED**

Storage Conditions:

Outside or detached storage is preferred. Inside storage should be in a standard flammable liquids storage warehouse, room, or cabinet. Separate from oxidizing materials.

[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 49-65]**PEER REVIEWED**

Temp: ambient; Venting: open (flame arrester) or pressure-vacuum
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Cleanup Methods:

1) REMOVE ALL IGNITION SOURCES. 2) VENTILATE AREA OF SPILL OR LEAK. 3) FOR SMALL QUANTITIES, ABSORB ON PAPER TOWELS. EVAPORATE IN SAFE PLACE (SUCH AS FUME HOOD). ... BURN PAPER IN SUITABLE LOCATION AWAY FROM COMBUSTIBLE MATERIALS. LARGE QUANTITIES CAN BE COLLECTED & ATOMIZED IN SUITABLE COMBUSTION CHAMBER.
[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) PublicationNo. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981. 1]**PEER REVIEWED**

Land spills should be contained; skimming equipment and/or sorbent (polyurethane) foams can be used. Use of activated carbon is recommended.
[Environment Canada; Tech Info for Problem Spills: Ethylbenzene p.83 (1982)]**PEER REVIEWED**

Water spills should be contained; skimming equipment and/or sorbent (polyurethane) foams can be used to remove the slick. Universal gelling agent can be used to solidify a trapped mass. Use of activated carbon on dissolved portion is recommended.
[Environment Canada; Tech Info for Problem Spills: Ethylbenzene p.83 (1982)]**PEER REVIEWED**

Environmental considerations: Land spill: Dig a pit, pond, lagoon, or holding area to contain liquid or solid material. /SRP: If time permits, pits, ponds, lagoons, soak holes, or holding areas should be sealed with an impermeable flexible membrane liner./ Dike surface flow using sand bags, foamed polyurethane, or foamed concrete. Absorb bulk liquid with fly ash, cement powder, sawdust, or commercial sorbents. Apply "universal" gelling agent to immobilize spill. Apply appropriate foam to diminish vapor and fire hazard.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 443]**PEER REVIEWED**

Environmental considerations - Air spill: Apply water spray or mist to knock down vapors.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 443]**PEER REVIEWED**

Environmental considerations: Water spill: Use natural barriers or oil spill control booms to limit spill travel. Use surface active agent (e.g., detergent, soaps, alcohols), if approved by EPA. Inject "universal" gelling agent to solidify encircled spill and increase effectiveness of booms. If dissolved, in region of 10

ppm or greater concentration, apply activated carbon at ten times the spilled amount. Remove trapped material with suction hoses. Use mechanical dredges or lifts to remove immobilized masses of pollutants and precipitates.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 443]**PEER REVIEWED**

ABSORB IN VERMICULITE, DRY SAND, EARTH OR SIMILAR MATERIAL
[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) PublicationNo. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981. 2]**PEER REVIEWED**

Disposal Methods:

Generators of waste (equal to or greater than 100 kg/mo) containing this contaminant, EPA hazardous waste number F003, must conform with USEPA regulations in storage, transportation, treatment and disposal of waste.
[40 CFR 240-280, 300-306, 702-799 (7/1/90)]**PEER REVIEWED**

Ethylbenzene is a waste chemical stream constituent which may be subjected to ultimate disposal by controlled incineration.
[USEPA; Engineering Handbook for Hazardous Waste Incineration p.2-6 (1981) EPA 68-03-3025]**PEER REVIEWED**

A good candidate for liquid injection incineration at a temperature range of 650 to 1,600 deg C and a residence time of 0.1 to 2 seconds. A good candidate for rotary kiln incineration at a temperature range of 820 to 1,600 deg C and residence times of seconds for liquids and gases, and hours for solids. A good candidate for fluidized bed incineration at a temperature range of 450 to 980 deg C and residence times of seconds for liquids and gases, and longer for solids.
[USEPA; Engineering Handbook for Hazardous Waste Incineration p.3-4 (1981) EPA 68-03-3025]**PEER REVIEWED**

The following wastewater treatment technologies have been investigated for ethylbenzene: Activated Carbon.
[USEPA; Management of Hazardous Waste Leachate, EPA Contract No.68-03-2766 p.E-146 (1982)]**PEER REVIEWED**

The following wastewater treatment technologies have been investigated for ethylbenzene: biological treatment.
[USEPA; Management of Hazardous Waste Leachate, EPA Contract No.68-03-2766 p.E-45 (1982)]**PEER REVIEWED**

The following wastewater treatment technologies have been investigated for ethylbenzene: stripping.
[USEPA; Management of Hazardous Waste Leachate, EPA Contract No.68-03-2766 p.E-96 (1982)]**PEER REVIEWED**

Occupational Exposure Standards:

OSHA Standards:

Permissible Exposure Limit: Table Z-1 8-Hr Time Weighted Avg: 100 ppm (435 mg/cu m).
[29 CFR 1910.1000 (7/1/99)]**PEER REVIEWED**

Vacated 1989 OSHA PEL TWA 100 ppm (435 mg/cu m); STEL 125 ppm (545 mg/cu m) is still enforced in some states.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 364]**PEER REVIEWED**

Threshold Limit Values:

8 Hr Time Weighted Avg (TWA) 100 ppm; Short Term Exposure Limit (STEL) 125 ppm
[American Conference of Governmental Industrial Hygienists. Threshold Limit Values (TLVs) for Chemical Substances and Physical Agents Biological Exposure Indices for 1998. Cincinnati, OH: ACGIH, 1998. 37]**PEER REVIEWED**

BEI (Biological Exposure Index): Biological Exposure Index (BEI) adoption (1986 edition): Determinant: Mandelic acid in urine; Sampling Time: end of shift at end of workweek; BEI: 1.5 g/g creatinine. The determinant is nonspecific, since it is observed after exposure to some other chemicals. These nonspecific tests are preferred because they are easy to use and usually offer a better correlation with exposure than specific tests. In such instances, a BEI for a specific, less quantitative biological determinant is recommended as a confirmatory test.
[American Conference of Governmental Industrial Hygienists. Threshold Limit Values (TLVs) for Chemical Substances and Physical Agents Biological Exposure Indices for 1998. Cincinnati, OH: ACGIH, 1998. 100]**PEER REVIEWED**

BEI (Biological Exposure Index): Determinant: Ethyl benzene in end-exhaled air . The biological determinant is an indicator of exposure to the chemical, but the quantitative interpretation of the measurements is ambiguous. (1986 adoption)
[American Conference of Governmental Industrial Hygienists. Threshold Limit Values (TLVs) for Chemical Substances and Physical Agents Biological Exposure Indices for 1998. Cincinnati, OH: ACGIH, 1998. 100]**PEER REVIEWED**

NIOSH Recommendations:

Recommended Exposure Limit: 10 Hr Time-Weighted Avg: 100 ppm (435 mg/cu m).
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 132]**PEER REVIEWED**

Recommended Exposure Limit: 15 Min Short-Term Exposure Limit: 125 ppm (545 mg/cu m).
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 132]**PEER REVIEWED**

Immediately Dangerous to Life or Health:

800 ppm
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 132]**PEER REVIEWED**

Other Occupational Permissible Levels:

Australia: 100 ppm, STEL 125 ppm, substance under review (1990); Federal Republic of Germany: 100 ppm, short-term level 200 ppm, 5 min, 8 times per shift, skin (1990); Sweden: 80 ppm, short-term value 100 ppm, 15 min (1989); United Kingdom: 100 ppm, 10-min STEL 125 ppm (1991).
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Volumes I,II, III. Cincinnati, OH: ACGIH, 1991. 584]**PEER REVIEWED**

Manufacturing/Use Information:

Major Uses:

USED IN ... THE PRODUCTION OF SYNTHETIC RUBBER ... AS A SOLVENT OR DILUENT, A COMPONENT OF AUTOMOTIVE AND AVIATION FUELS; MFR OF CELLULOSE ACETATE
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 2114]**PEER REVIEWED**

Ethylbenzene is mainly used as a precursor to styrene.
[Kirk-Othmer Encyclopedia of Chemical Technology. 4th ed. Volumes 1: New York, NY. John Wiley and Sons, 1991-Present.,p. V2 84]**PEER REVIEWED**

... SOLVENT-EG, FOR ALKYD SURFACE COATINGS, CHEM INT FOR DIETHYLBENZENE & ACETOPHENONE, FOR ETHYL ANTHRAQUINONE, FOR ETHYLBENZENE SULFONIC ACIDS (O-, M- & P-), FOR PROPYLENE OXIDE & ALPHA-METHYLBENZYL ALCOHOL, UNRECOVERED COMPONENT OF GASOLINE
[SRI]**PEER REVIEWED**

Used as an intermediate for the manufacture of the styrene monomer and as a resin solvent.
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 643]**PEER REVIEWED**

Intermediate for the production of diethylbenzene and acetophenone.
[Gerhartz, W. (exec ed.). Ullmann's Encyclopedia of Industrial Chemistry. 5th ed.Vol A1: Deerfield Beach, FL: VCH Publishers, 1985 to Present.,p. VA10 35]**PEER REVIEWED**

Used as a component of automotive and aviation fuels.

[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1342]**PEER REVIEWED**

Intermediate in production of styrene solvent.
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 1997. 461]**PEER REVIEWED**

Manufacturers:

Amoco Corporation, Hq, 200 East Randolph Drive, Chicago, IL 60601, (312) 856-6111; Subsidiary: Amoco Chemical Company (address same as Hq), (312) 856-3200; Chemical & Specialty Product Group; Production site: Texas City, TX 77592
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 593]**PEER REVIEWED**

ARCO Chemical Co., Hq, 3801 W. Chester Pk., Newtown Square, PA 19073; Production site: Channelview, TX 77530
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 583]**PEER REVIEWED**

Chevron Chemical Co., 6001 Bollinger Canyon Rd., San Ramon, CA 94583, (925) 842-5500; Production site: St. James, LA 70086
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 593]**PEER REVIEWED**

Cos-Mar, Inc., Hq, PO Box 11, Carville, LA 70721, (504) 642-5454; Production site: Carville, LA 70721
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 593]**PEER REVIEWED**

Dow Chemical USA, Hq, 2020 Dow Center, Midland, MI 48674, (517) 636-1000; Production site: Freeport, TX 77541
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 593]**PEER REVIEWED**

Huntsman Corp., 3040 Post Oak Blvd., Houston, TX 77056, (713) 235-6000; Production site: Odessa, TX 79760
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 593]**PEER REVIEWED**

Sterling Chemicals, Inc., Hq, 333 Clay St., Suite 3700, Houston, TX 77002, (713) 650-3700; Production site: Texas City, TX 77590
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 593]**PEER REVIEWED**

Westlake Styrene Corp., 2801 Post Oak Blvd., Suite 200, Houston, TX 77056, (713) 877-1924; Production site: Lake Charles, LA 70602-3089
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 593]**PEER REVIEWED**

Methods of Manufacturing:

Prepared by dehydrogenation of naphthenes or from catalytic cyclization and aromatization.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1342]**PEER REVIEWED**

ALKYLATION OF BENZENE WITH ETHYLENE IN LIQUID PHASE USING ALUMINUM CHLORIDE CATALYST OR IN VAPOR PHASE USING PHOSPHORIC ACID OR ALUMINA-SILICA CATALYST; RECOVERY FROM MIXED XYLENES VIA FRACTIONATION
[SRI]**PEER REVIEWED**

Prepd from acetophenone
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 643]**PEER REVIEWED**

Produced by alkylation of benzene with ethylene using acidic catalysts and can be carried out in the liquid or vapor phase.
[Kirk-Othmer Encyclopedia of Chemical Technology. 4th ed. Volumes 1: New York, NY. John Wiley and Sons, 1991-Present.,p. V22 957]**PEER REVIEWED**

Produced via the use of zeolite catalyst, ZSM-5, in a process called the Mobil-Badger vapor phase ethylbenzene process.
[Kirk-Othmer Encyclopedia of Chemical Technology. 4th ed. Volumes 1: New York, NY. John Wiley and Sons, 1991-Present.,p. V22 961]**PEER REVIEWED**

(1) By heating benzene and ethylene in the presence of aluminum chloride, with subsequent distillation; (2) by fractionation directly from the mixed xylene stream in petroleum refining.
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 1997. 461]**PEER REVIEWED**

General Manufacturing Information:

In most processes, ethylbenzene is not recovered because of high energy costs.
[Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984.,p. V24 717 (1983)]**PEER REVIEWED**

Ethylbenzene is recovered from benzene-toluene-xylene (BTX) processing.
[Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984.,p. V4 64 (1978)]**PEER REVIEWED**

19th-highest-volume chemical produced in the U.S. (1995).
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 1997. 461]**PEER REVIEWED**

Formulations/Preparations:

GRADE: TECHNICAL 99.0%; PURE 99.5%; RESEARCH 99.98%.
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Grade: Technical, pure, research
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 1997. 461]**PEER REVIEWED**

Consumption Patterns:

Intermediate for styrene monomer production, more than 99%; the remainder is exported or sold as solvent (1984).
[CHEMICAL PROFILE: Ethylbenzene, 1984]**PEER REVIEWED**

Styrene, 97%; Miscellaneous, 3% (1983) /Estimate/
[CHEMICAL PRODUCTS SYNOPSIS: Ethylbenzene, 1983]**PEER REVIEWED**

CHEMICAL PROFILE: Ethylbenzene. Intermediate for styrene monomer production, over 99%. The remainder is used in solvent applications.
[Kavaler AR; Chemical Marketing Reporter 236 (8): 50 (1989)]**PEER REVIEWED**

CHEMICAL PROFILE: Ethylbenzene. Demand: 1988: 9,935 million lb; 1989: 10,230 million lb; 1993 /projected/: 11,500 million lb. (Imports and exports are both minor, each one on the order of 200 million lb.)
[Kavaler AR; Chemical Marketing Reporter 236 (8): 50 (1989)]**PEER REVIEWED**

Precursors for styrene production, more than 99 percent. The remainder is used in solvent applications.
[Chemical Marketing Reporter; Chemical Profile Ethylbenzene. April 27, 1998. p. 57. NY,NY: Schnell Pub Co (1998)]**PEER REVIEWED**

U. S. Production:

(1977) 8.3X10+9 lb
[United States International Trade Commission. Synthetic Organic Chemicals-- United States Production and Sales, 1981. USITC Publications 1291 Washington, DC: United States InternationalTrade Commission, 1981. 27]**PEER REVIEWED**

(1980) 3.5 x 10+12 g
[Kavaler, A.R. (ed.). Chemical Marketing Reporter. New York, NY: Schnell Publishing Co., Inc., 1984]**PEER REVIEWED**

(1981) 3.5 x 10+12 g
[Kavaler, A.R. (ed.). Chemical Marketing Reporter. New York, NY: Schnell Publishing Co., Inc., 1984]**PEER REVIEWED**

(1977) 3.77X10+12 G
[SRI]**PEER REVIEWED**

(1982) 3.15X10+12 G
[SRI]**PEER REVIEWED**

(1985) 3.35X10+12 g
[USITC, SYN ORG CHEM-US PROD/SALES (1985) p.29]**PEER REVIEWED**

(1988) 9.9X10+9 lb
[United States International Trade Commission. Synthetic Organic Chemicals- United States Production and Sales, 1988. USITC Publication 1989. Washington,DC: United States International Trade Commission, 1989.,p. 3-2]**PEER REVIEWED**

(1990) 8.37 billion lb
[Chem & Engineering News 70 (15): 17 (4/13/92)]**PEER REVIEWED**

(1991) 8.87 billion lb
[Chem & Engineering News 71 (15): 11 (4/12/93)]**PEER REVIEWED**

(1992) 11.11 billion lb
[Chem & Engineering News 72 (15): 13 (4/11/94)]**PEER REVIEWED**

(1993) 11.76 billion lb
[Chem & Engineering News 72 (15): 13 (4/11/94)]**PEER REVIEWED**

(1993) 4,233,835 kg
[United States International Trade Commission. Synthetic Organic Chemicals - United States Production and Sales, 1993. USITC Publication 2810, Nov. 1994. Washington, D.C.,p. 3-15]**PEER REVIEWED**

1997: 12.9 billion pounds; 1998 13 billion pounds; 2002 15 billion pounds. (Includes exports, which amounted to 126 million pounds in 1996, but not imports which totaled 16 million pounds in that year).
[Chemical Marketing Reporter; Chemical Profile Ethylbenzene. April 27, 1998. p. 57. NY,NY: Schnell Pub Co (1998)]**PEER REVIEWED**

Growth: Historical (1988-1997): 2.5 percent per year; future: 3 percent per year through 2002.
[Chemical Marketing Reporter; Chemical Profile Ethylbenzene. April 27, 1998. p. 57. NY,NY: Schnell Pub Co (1998)]**PEER REVIEWED**

U. S. Imports:

(1978) 1.53X10+10 G
[SRI]**PEER REVIEWED**

(1981) 2.09X10+10 G
[SRI]**PEER REVIEWED**

US General Imports entered under schedule 4, pt 1B, of the TSUS (1983). Quantity of ethylbenzene:

87,201,615 lbs.
[USITC. IMPORTS OF BENZENOID CHEM & PROD (1983) p.18]**PEER REVIEWED**

(1996) 16 million pounds
[Chemical Marketing Reporter; Chemical Profile Ethylbenzene. April 27, 1998. p. 57. NY,NY: Schnell Pub Co (1998)]**PEER REVIEWED**

U. S. Exports:

(1978) 8.59X10+10 G
[SRI]**PEER REVIEWED**

(1983) 4.84X10+10 G
[SRI]**PEER REVIEWED**

(1985) 7.49X10+10 g
[BUREAU OF THE CENSUS, US EXPORTS, SCHEDULE E, (1985) p.2-69]**PEER REVIEWED**

(1996) 126 million pounds
[Chemical Marketing Reporter; Chemical Profile Ethylbenzene. April 27, 1998. p. 57. NY,NY: Schnell Pub Co (1998)]**PEER REVIEWED**

Laboratory Methods:

Clinical Laboratory Methods:

IN BLOOD BY ULTRAVIOLET-SPECTROPHOTOMETRIC METHOD.
[Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965. 91]**PEER REVIEWED**

An automated high performance liquid chromatographic method for the direct determination of urinary concentrations of phenyl glyoxylic acid and mandelic acid, metabolites of styrene or ethylbenzene, is described. The method is simple and specific. Urine can be analyzed without solvent extraction. Analysis can be performed satisfactorily within 15 minutes for samples containing hippuric acid, o-, m- and p-methyl hippuric acids, phenyl glyoxylic acid, and mandelic acid, and within 15 minutes for those containing hippuric acid, phenyl glyoxylic acid and mandelic acid.
[Ogata M, Taguchi T; Int Arch Occup Environ Health 59 (3): 263-72 (1987)]**PEER REVIEWED**

Analytic Laboratory Methods:

EPA Method 624. Purge-and-Trap Gas Chromatography/Mass Spectrometry for the analysis of purgeable organics including ethylbenzene in the municipal and industrial discharges. Under the prescribed conditions, for ethylbenzene the method has a detection limit of 7.2 ug/l. Precision and method accuracy were found to be directly related to the concentration of the analyte and essentially independent of the sample matrix.
[40 CFR 136 (7/1/91)]**PEER REVIEWED**

EPA Method 1624. Isotope Dilution Purge-and-Trap Gas Chromatography/Mass Spectrometry. This

method is applicable for the determination of volatile organic compounds in municpal and industrial discharges. By adding a known amount of a labeled compound to every sample prior to purging, a correction of recovery of the pollutant can be made. If labeled compounds are not available, an internal standard method is used. Under the prescribed conditions, for both the labeled, and unlabeled ethylbenzene the method has a minimum detection level 10 ug/l.The established acceptance performance criteria at 20 ug/l is 9.6 ug/l for the standard deviation of the recovery, with the average recovery of 15.6 to 28.5 ug/l and the labeled cmpd recovery ranging from below detection to 203%.
[40 CFR 136 (7/1/91)]**PEER REVIEWED**

EPA Method 602. Purge-and-Trap Gas Chromatography with photoionization detection for the determination of purgeable aromatics including ethylbenzene in municipal and industrial discharges. Under the prescribed conditionss for ethylbenzene the detection limit is 0.2 ug/l. The method is applicable for use in the concentration range from the method detection limit to times that limit. Precision and method accuracy were found to be directly related to the concentration of the analyte essentially independent of the sample matrix.
[40 CFR 136 (7/1/91)]**PEER REVIEWED**

EPA Method 524.2. Purge-and-Trap Gas Chromatography/Mass Spectrometry for the determination of volatile aromatic compounds in water including finished drinking water, raw source water, and drinking water in any treatment stage. For ethylbenzene the method has a detection limit of 0.06 ug/l and a relative standard deviation of 8.6% with a wide bore capillary column, and a method detection limit of 0.03 ug/l and a relative standard deviation of 5.3% with a narrow bore capillary column.
[USEPA; Methods for the Determinatioon of Organic Compounds in Finished Drinking Water and Raw Source Water (19860]**PEER REVIEWED**

EPA Method 503.1. Purge-and-Trap Gas Chromatography with a Photoionization Detector. The method is applicable for the determination of volatile aromatic and unsaturated organic compounds in finished drinking water, raw source water, or drinking water in any treatment stage. For ethylbenzene the method has a detection limit of 0.002 ug/l and a relative standard deviation of 8.5%. Overall precision and method accuracy were found to be directly related to the concentration of the analyte essentially independent of sample matrix.
[USEPA; Methods for the Determination of Organic Compouds in Finished Drinking Water and Raw Source Water (1986)]**PEER REVIEWED**

EPA Method 502.2: Purge-and-Trap Capillary Column Gas Chromatography with Photoionization and Electrolytic Conductivity Detectors in Series. The method is applicable for the determination of volatile organic compounds in finished drinking water, raw source water, or drinking water in any treatment stage. For ethylbenzene the method has a detection limit of 0.005 ug/l, a percent recovery of 101%, and a standard deviation of 1.4 using the photoionization detector; and there is no data given for the following: the method detection limit, a percent recovery, or the standard deviation of recovery using the electrolytic conductivity detector.
[USEPA; Methods for the Determination of Organic Compounds in Finished Drinking Water and Raw Source Water (1986)]**PEER REVIEWED**

NIOSH Method 1501. Determination of Aromatic Hydrocarbons by Gas Chromatography with Flame Ionization Detection.
[U.S. Department of Health and Human Services, Public Health Service,

Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSH Manual of Analytical Methods. 4th ed.Methods A-Z & Supplements. Washington, DC: U.S. Government Printing Office, Aug 1994.]**PEER REVIEWED**

EPA Method 8240. Gas Chromatography/Mass Spectrometry for the determination of volatile organics. This method can be used to quantify most volatile organic compounds including ethylbenzene that have boiling points below 200 deg C and are insoluble or slightly soluble in water. The detection limit is not given. Precision and method accuracy were found to be directly related to the concentration of the analyte and essentially independent of the sample matrix.
[USEPA/Office of Solid Waste (OSW); Test Methods for Evaluating Solid Waste, Physical/Chemical Methods SW846 Methods (1986)]**PEER REVIEWED**

EPA Method 8260. Gas Chromatography/Mass Spectrometry for the determination of volatile organic compounds. This method can be used to quantitate most volatile organic compounds including ethylbenzene that have boiling points below 200 deg C and are insoluble or slightly soluble in water. Under the prescribed conditions for ethylbenzene, the method has a detection limit of 0.06 ug/l, a percent recovery of 99%, and a percent relative standard deviation of 8.6% using a wide bore capillary column; and a detection limit of 0.03 ug/l, a percent recovery of 99%, and a percent relative standard deviation of 5.3% using a narrow bore capillary column.
[USEPA/Office of Solid Waste (OSW); Test Methods for Evaluating Solid Waste, Physical/Chemical Methods SW846 Methods (1986)]**PEER REVIEWED**

OSW Method 8240B. Determination of Volatile Organics Compounds by Gas Chromatography/Mass Spectrometry (GC/MS).
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

OSW Method 5021. Volatile Organic Compounds in Soils and Other Solid Matrices Using Equilibrium Headspace Analysis.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

OSW Method 8020A. Determination of Aromatic Volatile Organics by Gas Chromatography.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

OSW Method 8021A. Analysis of Halogenated and Aromatic Volatiles By Gas Chromatography using Electrolytic Conductivity and Photoionization Detectors in Series: Capillary Column Technique.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

OSW Method 8021A. Halogenated and Aromatic Volatiles By Gas chromatography using Electrolytic Conductivity and Photoionization Detectors in Series: Capillary Technique.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

OSW Method 8240B. Determination of Volatile Organic Compounds by Gas Chromatography/Mass Spectrometry (GC/MS).
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

OSW Method 8260A. Determination of Volatile Organic Compounds by Gas Chromatography/Mass Spectrometry (GC/MS): Capillary Column Technique.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

OSW Method 8260B. Volatile Organic Compounds by Gas Chromatography/Mass Spectrometry (GC/MS): Capillary Column Technique.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

OSW Method 5041. Analysis of Sorbent Cartridges From Volatile Organic Sampling Train by using the Wide-Bore Capillary Column Technique.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

OSW Method 5041A. Protocol for Desorption of Sorbent Cartridges from Volatile Organic Sampling Train (VOST): Wide-Bore Capillary GC/MS Technique.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method OA-002-1. Volatile Organic Compounds by GC/MS Analysis of Tenax/CMS Cartridge and Summa Canister Samples.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VA-001-1. Volatile Organic Compounds (VOCs) in Air Sampled by Sorbent Tubes and Analyzed by Purge and Trap GC.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VA-003-1. Volatile Organic Compounds (VOCs) in Air by Portable GC/PID.

[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VA-005-1. Volatile Organic Compounds (VOCs) in Ambient Air by Purge and Trap Gas Chromatography.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VA-006-1. Volatile Organic Compounds (VOCs) in Ambient Air by Direct Portable GC/PID.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VA-008-1. Volatile Organic Compounds (VOCs) in Ambient Air by Portable GC/PID with Direct Sampling via Pump and Sample Loop.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VG-001-1. Volatile Organics in Soil Gas - Adsorbent Tube Method.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VG-006-1. Volatile Organic Compounds (VOCs) in Ambient Air by Purge and Trap GC.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VG-007-1. Halogenated and Aromatic Volatile Organic Compounds (VOCs) in Air and Soil Gas Sampled by Sorbent Tubes and Analyzed by Purge and Trap GC/ELCD/PID.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VG-008-1. Volatile Organic Compounds (VOCs) in Soil Gas sampled by Tenax Tubes and Analyzed by Thermal Desorption GC/PID/ELCD.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VG-010-1. Volatile Organic Compounds (VOCs) in Soil Gas by Direct Portable GC.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VG-011-1. Halogenated and Aromatic Volatile Organic Compounds (VOCs) in Whole Gas Analyzed by Purge and Trap GC/ELCD/PID.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VW-001-1. Volatile Organic Compounds (VOCs) in Water by Purge and Trap GC/PID/ELCD.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VW-002-1. Volatile Organic Compounds (VOCs) in Water by Automated Headspace GC/PID/ELCD.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VW-003-1. Volatile Organic Compounds (VOCs) in Water by Automated Headspace GC/PID/ELCD (Internal Standard).
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VW-004-1. Volatile Organic Compounds (VOCs) in Water by Manual Headspace Portable GC/PID.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VW-008-1. Volatile Organic Compounds (VOCs) in Water by Purge and Trap GC.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VW-010-1. Field Screening for Volatile Organic Compounds (VOCs) in Water and Soil by Headspace GC/PID (Photovac 10S10).
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VW-014-1. Volatile Organic Compounds (VOCs) in Water by Purge and Trap GC/PID/ELCD.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VS-001-1. Volatile Organic Compounds (VOCs) in Soil by Purge and Trap GC/PID/ELC.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version

1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VS-002-1. Volatile Organic Compounds (VOCs) in Soil and Sediment by Automated Headspace GC/PID/ELCD.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VW-010-1. Field Screening for Volatile Organic Compounds (VOCs) in Water and Soil by Headspace GC/PID (Photovac 10S10).
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

CLP Method LC_VOA. Analysis of Water for Low concn Volatile Organic Compounds by Gas Chromatography/Mass Spectroscopy.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

CLP Method MC_VOA. Analysis of Volatile Organics in Multi-Concentration Water Samples by Gas Chromatography with a Mass Spectrometer.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

CLP Method MC_VOA. Analysis of Volatile Organics in Low concn Soil Samples by Gas Chromatography with a Mass Spectrometer.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

CLP Method MC_VOA. Analysis of Volatile Organics in Medium concn Soil Samples by Gas Chromatography with a Mass Spectrometer.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

DOE Method OS040. Rapid Determination Of Volatile Organic Contaminants in Water and Soils by Direct Purge Mass Spectrometry.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

DOE Method OS040. Rapid Determination Of Volatile Organic Contaminants in Water and Soils by Direct Purge Mass Spectrometry.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER

REVIEWED**

DOE Method OS060. Immunoassay for Petroleum Fuel Hydrocarbons in Soil.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

EAD Method 1624. Volatile Organic Compounds by Isotope Dilution GCMS.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

EAD Method 1624. Volatile Organic Compounds by Isotope Dilution GCMS.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

EMSLC Method 502.2. Volatile Organic Compounds in Water by Purge and Trap Capillary Column Gas Chromatography with Photoionization and Electrolytic Conductivity Detectors in Series.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

EMSLC Method 503.1. Volatile Aromatic and Unsaturated Organic Compounds in Water by Purge and Trap Gas Chromatography.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

EMSLC Method 524.1. Measurement of Purgeable Organic Compounds in Water by Packed Column Gas Chromatography and Mass Spectrometry.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

EMSLC Method 524.2 Measurement of Purgeable Organic Compounds in Water by Capillary Column Gas Chromatography/Mass Spectrometry.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

EMSLC Method 602. Purgeable Aromatics in Wastewater by Gas Chromatography with Photoionization Detection.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

EMSLC Method 624. Protocol for the Analysis of Purgeable Organic Priority Pollutants in Industrial and Municipal Wastewater.

[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

EMSLC Method 624-S. Analysis of Purgeable Organic Priority Pollutants in Industrial and Municipal Wastewater Treatment Sludge.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

SFSAS Method SFSAS_7. Determination of Purgeable Organics in Sediment.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VS-006-1. Volatile Organic Compounds (VOCs) in Soil and Water by Purge and Trap GC.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VW-011-1. Field Screening for Volatile Organic Compounds (VOCs) in Water and Soil by Purge and Trap GC/PID/ELCD.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

CLP Method OHC. Organics Analysis, Multi-Media, High-Concentration.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

SFSAS Method SFSAS_29. Extraction and Analysis of Organics in Biological Tissue.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

SFSAS Method SFSAS_5. Analysis of Fish for Volatile Organics by Purge and Trap Analysis.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

Sampling Procedures:

AIR SAMPLES WERE COLLECTED IN TEFLON LOOP (3.0 ML).
[IMAMURA K ET AL; BUNSEKI KAGAKU 28 (9): 549 (1979)]**PEER REVIEWED**

NIOSH Method 1501. Analyte: Ethylbenzene. Matrix: Air. Sampler: Solid sorbent tube (coconut shell charcoal, 100 mg/50 mg). Flow Rate: less or equal to 0.2 l/min. Sample Size: 10-24 liters. Shipment: no special specifications. Sample Stability: not determined.

[U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. 1501-1]**PEER REVIEWED**

Special References:

Special Reports:

HALEY TJ, A REVIEW OF LITERATURE ON ETHYLBENZENE; DANGEROUS PROP IND MATER REP 1(6) 2 (1981). A REVIEW WITH 39 REFERENCES ON CHEMISTRY, METABOLISM, PHARMACOLOGY & TOXICITY OF ETHYLBENZENE.

USEPA; Ambient Water Quality Criteria Document: Ethylbenzene (1980) EPA No. 440/5-8-048.

Environment Canada; Tech Info for Problem Spills: Ethylbenzene (Draft) (1982)

Fishbein L; Ethylbenzene in An Overview of Environmental and Toxicological Aspects of Aromatic Hydrocarbons; Sci Total Environ 44 (3): 269-88 (1985)

Forrest RG et al; Hazardous Mater Spills Conference Proc, Prev, Behav, Control Cleanup Spills Waste Sites (1984) 17-23

Chemical Review: Ethylbenzene; Dangerous Prop Ind Mater Rep 7 (2): 13-35 (1987)

DHHS/ATSDR; Toxicological Profile for Ethylbenzene (1990) ATSDR/TP-90/15

USEPA/ECAO; Ambient Water Quality Criteria Document: Addendum for Ethylbenzene. Final Draft (12/89) ECAO Pub. ECAO-CIN-647

DHHS/NTP; NTP Report on the Toxicity Studies of Ethylbenzene in F344/N Rats and B6C3F1 Mice (Inhalation Studies) NTP Tox 10 (1992)

Toxicology & Carcinogenesis Studies of Ethylbenzene in F344/N Rats and B6C3F1 Mice p.5 Technical Report Series No. 466 (1999) NIH Publication No. 99-3956 U.S. Department of Health and Human Services, National Toxicology Program, National Institute of Environmental Health Sciences, Research Triangle Park, NC 27709

Synonyms and Identifiers:

Synonyms:

AETHYLBENZOL (GERMAN)
PEER REVIEWED

BENZENE, ETHYL-
PEER REVIEWED

EB
PEER REVIEWED

ETHYLBENZEEN (DUTCH)
PEER REVIEWED

ETHYL BENZENE
PEER REVIEWED

ETHYLBENZOL
PEER REVIEWED

ETILBENZENE (ITALIAN)
PEER REVIEWED

ETYLOBENZEN (POLISH)
PEER REVIEWED

NCI-C56393
PEER REVIEWED

PHENYLETHANE
PEER REVIEWED

Formulations/Preparations:

GRADE: TECHNICAL 99.0%; PURE 99.5%; RESEARCH 99.98%.
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Grade: Technical, pure, research
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 1997. 461]**PEER REVIEWED**

Shipping Name/ Number DOT/UN/NA/IMO:

UN 1175; Ethylbenzene

IMO 3.2; Ethylbenzene

Standard Transportation Number:

49 091 63; Ethylbenzene

EPA Hazardous Waste Number:

F003; A hazardous waste from nonspecific sources when a spent solvent.

RTECS Number:

NIOSH/DA0700000

Administrative Information:

Hazardous Substances Databank Number: 84

Last Revision Date: 20010130

Last Review Date: Reviewed by SRP on 1/29/2000

Update History:

Complete Update on 01/30/2001, 2 fields added/edited/deleted.
Complete Update on 09/12/2000, 1 field added/edited/deleted.
Complete Update on 08/04/2000, 91 fields added/edited/deleted.
Field Update on 02/08/2000, 1 field added/edited/deleted.
Field Update on 02/02/2000, 1 field added/edited/deleted.
Field Update on 11/18/1999, 1 field added/edited/deleted.
Field Update on 09/21/1999, 1 field added/edited/deleted.
Field Update on 08/24/1999, 1 field added/edited/deleted.
Complete Update on 03/29/1999, 3 fields added/edited/deleted.
Field Update on 03/19/1999, 1 field added/edited/deleted.
Field Update on 03/17/1999, 1 field added/edited/deleted.
Complete Update on 02/24/1999, 2 fields added/edited/deleted.
Complete Update on 01/20/1999, 1 field added/edited/deleted.
Complete Update on 11/12/1998, 1 field added/edited/deleted.
Complete Update on 09/03/1998, 1 field added/edited/deleted.
Complete Update on 06/02/1998, 1 field added/edited/deleted.
Complete Update on 02/25/1998, 1 field added/edited/deleted.
Complete Update on 10/17/1997, 1 field added/edited/deleted.
Complete Update on 03/27/1997, 2 fields added/edited/deleted.
Complete Update on 02/26/1997, 1 field added/edited/deleted.
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Complete Update on 10/19/1995, 1 field added/edited/deleted.
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Complete Update on 08/20/1993, 1 field added/edited/deleted.

Complete Update on 08/10/1993, 1 field added/edited/deleted.
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Complete Update on 04/30/1993, 1 field added/edited/deleted.
Complete Update on 02/05/1993, 1 field added/edited/deleted.
Field update on 12/10/1992, 1 field added/edited/deleted.
Complete Update on 09/14/1992, 72 fields added/edited/deleted.
Field Update on 09/04/1992, 1 field added/edited/deleted.
Field Update on 09/04/1992, 1 field added/edited/deleted.
Complete Update on 08/17/1992, 72 fields added/edited/deleted.
Field Update on 07/29/1992, 1 field added/edited/deleted.
Field Update on 05/29/1992, 1 field added/edited/deleted.
Field Update on 04/16/1992, 1 field added/edited/deleted.
Field Update on 01/13/1992, 1 field added/edited/deleted.
Field Update on 09/12/1991, 1 field added/edited/deleted.
Field Update on 09/10/1991, 1 field added/edited/deleted.
Field Update on 09/10/1991, 1 field added/edited/deleted.
Complete Update on 07/09/1991, 2 fields added/edited/deleted.
Complete Update on 10/10/1990, 1 field added/edited/deleted.
Complete Update on 04/16/1990, 2 fields added/edited/deleted.
Field update on 03/06/1990, 1 field added/edited/deleted.
Complete Update on 01/11/1990, 4 fields added/edited/deleted.
Field Update on 05/05/1989, 1 field added/edited/deleted.
Complete Update on 12/09/1988, 2 fields added/edited/deleted.
Complete Update on 09/23/1988, 1 field added/edited/deleted.
Complete Update on 08/15/1988, 104 fields added/edited/deleted.
Complete Update on 10/03/1986

Record Length: 199409

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Human Health Effects:

Toxicity Summary:

The acute toxicity of ethylbenzene to algae, aquatic invertebrates and fish is moderate. ... No information is available regarding chronic exposure of aquatic organisms to ethylbenzene. There is limited information regarding the toxicity of ethylbenzene to bacteria ... There are no data for terrestrial plants, birds, or wild mammals. Human exposure to ethylbenzene occurs mainly by inhalation; 40-60% of inhaled ethylbenzene is retained in the lung. Ethylbenzene is extensively metabolized, mainly to mandelic and phenylglyoxylic acids. These urinary metabolites can be used to monitor human exposures. Ethylbenzene has low acute and chronic toxicity for both animals and humans. It is toxic to the central nervous system and is an irritant of mucous membranes and the eyes. ... Ethylbenzene is an inducer of liver microsomal enzymes. It is not mutagenic or teratogenic ... No information is available on reproductive toxicity or carcinogenicity of ethylbenzene. A guidance value of 22 mg/ cu m (5 ppm) has been calculated from animal studies. /This value would correspond to a weekly absorbed dose (daily ventilation of 20 cu m with 60% retention) of about 2000 mg./ The estimated exposure of the general population (even in the worst case situation) is below this guidance value. Long term occupational exposure to ethylbenzene concentrations estimated to be of this order of magnitude did not cause adverse health effects in workers.

[Environmental Health Criteria 186: Ethylbenzene pp. 19-20 (1996) by the International Programme on Chemical Safety (IPCS) under the joint sponsorship of the United Nations Environment Programme, the International Labour Organisation and the World Health Organization.]**QC REVIEWED**

Evidence for Carcinogenicity:

CLASSIFICATION: D; not classifiable as to human carcinogenicity. BASIS FOR CLASSIFICATION: nonclassifiable due to lack of animal bioassays and human studies. HUMAN CARCINOGENICITY DATA: None. ANIMAL CARCINOGENICITY DATA: None.

[U.S. Environmental Protection Agency's Integrated Risk Information System (IRIS) on Ethylbenzene (100-41-4) Available from: http://www.epa.gov/ngispgm3/iris on the Substance File List as of March 15, 2000]**PEER REVIEWED**

Human Toxicity Excerpts:

PROLONGED EXPOSURE TO ... VAPORS MAY RESULT IN FUNCTIONAL DISORDERS, INCREASE IN DEEP REFLEXES, IRRITATION OF UPPER RESPIRATORY TRACT, HEMATOLOGICAL DISORDERS (LEUKOPENIA AND LYMPHOCYTOSIS, IN PARTICULAR) AND ... HEPATOBILIARY COMPLAINTS.

[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office,

1983. 2114]**PEER REVIEWED**

... ASPIRATION OF EVEN A SMALL AMT OF ETHYLBENZENE MAY CAUSE SEVERE INJURY, SINCE ITS LOW VISCOSITY AND SURFACE TENSION WILL CAUSE IT TO SPREAD OVER A LARGE SURFACE OF PULMONARY TISSUE. ...
[Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965. 92]**PEER REVIEWED**

Produces an irritant effect from chronic inhalation at 100 ppm (0.492 mg/L)/8 hr. /From table/
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1344]**PEER REVIEWED**

... /IT HAS BEEN/ SHOWN THAT CONCN OF 1 MG/L & EVEN 0.1 MG/L MAY BE DANGEROUS & MAY PRODUCE FUNCTIONAL & ORGANIC DISTURBANCES (NERVOUS SYSTEM DISORDERS, TOXIC HEPATITIS & UPPER RESP TRACT COMPLAINTS). CONCN AS LOW AS 0.01 MG/L MAY LEAD TO ... INFLAMMATION OF UPPER RESP TRACT MUCOSA.
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 2114]**PEER REVIEWED**

Ethyl benzene vapor has a transient irritant effect on human eyes at 200 ppm in air. At 1000 ppm on the first exposure it is very irritating and causes tearing, but tolerance rapidly develops. At 2000 ppm eye irritation and lacrimation are immediate and severe; 5000 ppm causes intolerable irritation of the eyes and nose.
[Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986. 413]**PEER REVIEWED**

ETHYLBENZENE IS MORE VOLATILE THAN STYRENE AND ITS MANUFACTURE IS ACCOMPANIED BY A GREATER HAZARD OF ACUTE POISONING. ...
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 2114]**PEER REVIEWED**

Skin, Eye and Respiratory Irritations:

... CHARACTERIZED ... AS MOST SEVERE IRRITANT OF THE BENZENE SERIES.
[American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices. 5th ed. Cincinnati, OH:American Conference of Governmental Industrial Hygienists, 1986. 244]**PEER REVIEWED**

A concn of 200 ppm causes eye irritation. A concn of 100 ppm for 8 hr caused irritative effects in a human.
[Cleland, J.G., G.L. Kingsbury. Multimedia Environmental Goals for Environmental Assessment. Volume 1. EPA-600/7-77-136a. Research Triangle Park, NC: EPA, Nov. 1977.,p. E-148]**PEER REVIEWED**

EXPOSURE TO CONCN OF 5000 PPM /24.6 MG/L/ ... CAUSES INTOLERABLE IRRITATION OF

EYES, MUCOUS MEMBRANES & NOSE.
[Patty, F. (ed.). Industrial Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New York: Interscience Publishers, 1963. 1232]**PEER REVIEWED**

HAZARD WARNING: ... exposure to 21.5 g/cu m (5000 ppm) ethylbenzene for a few seconds gives intolerable irritation of nose, eyes, and throat.
[Environmental Health Criteria 186: Ethylbenzene pp. 67 (1996) by the International Programme on Chemical Safety (IPCS) under the joint sponsorship of the United Nations Environment Programme, the International Labour Organisation and the World Health Organization.]**QC REVIEWED**

Medical Surveillance:

... EMPLOYMENT EXAMINATION SHOULD ENSURE THAT PERSONS WITH LIVER, KIDNEY, NERVOUS SYSTEM, BLOOD AND HEMOPOIETIC-ORGAN DISORDERS ARE /PROTECTED FROM EXPOSURE/ ... WOMEN WITH OVULATION AND MENSTRUAL CYCLE DISORDERS SHOULD ALSO BE /PROTECTED/.
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 2114]**PEER REVIEWED**

Consider the points of attack (eyes, upper respiratory system, skin, central nervous system) in placement and periodic physical examinations.
[Sittig, M. Handbook of Toxic and Hazardous Chemicals and Carcinogens, 1985. 2nd ed. Park Ridge, NJ: Noyes Data Corporation, 1985. 413]**PEER REVIEWED**

Populations at Special Risk:

IN PERSONS WITH IMPAIRED PULMONARY FUNCTION, ESP THOSE WITH OBSTRUCTIVE AIRWAY DISEASES, BREATHING ETHYL BENZENE MIGHT CAUSE EXACERBATION OF SYMPTOMS DUE TO ITS IRRITANT PROPERTIES OR PSYCHIC REFLEX BRONCHOSPASM.
[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) PublicationNo. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981.]**PEER REVIEWED**

PERSONS WITH ... EXISTING SKIN DISORDERS MAY BE MORE SUSCEPTIBLE TO EFFECTS. ...
[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) PublicationNo. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981.]**PEER REVIEWED**

... PERSONS WITH LIVER, KIDNEY, NERVOUS SYSTEM, BLOOD AND HEMOPOIETIC-ORGAN DISORDERS. ... WOMEN WITH OVULATION AND MENSTRUAL CYCLE DISORDERS. ...

[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 2114]**PEER REVIEWED**

Probable Routes of Human Exposure:

NIOSH (NOES Survey 1981-1983) has statistically estimated that 80,726 workers (21,785 of these are female) are potentially exposed to ethylbenzene in the US(1). Occupational exposure to ethylbenzene may occur via inhalation at municipal waste composting facilities where the air concn was found to be 78,000-178,000 ug/cu m(2),and through inhalation and dermal contact with this compound at worplaces where ethylbenzene is produced or used(SRC). The general population may be exposed to ethylbenzene via inhalation of ambient air, ingestion of foods and fish, and drinking contaminated water, and dermal contact with this compound and other products such as gasoline which contains ethylbenzene(SRC).
[(1) NIOSH; National Occupational Exposure Survey (NOES) (1983) (2) Eitzer BD; Environ Sci Technol 29: 896-902 (1995)]**PEER REVIEWED**

Body Burden:

Ethylbenzene was detected, not quantified, in 8 of 8 samples of mother's milk from 4 US urban areas(1). 16.5% of 387 expired air samples taken from 54 normal, healthy, urban volunteers were positive for ethylbenzene concn with an avg of 1.8 ng/l expired air(2). Whole blood samples from 250 subjects ranged in ethylbenzene concns from not detected to 59 ppb, with an avg of 1.0 ppb(3).
[(1) Pellizzari ED et al; Bull Environ Contam Toxicol 28: 322-8 (1982) (2) Krotoszynski BK et al; J Anal Toxicol 3: 225-34 (1979) (3) Antoine SR et al; Bull Environ Contam Toxicol 36: 364-71 (1986)]**PEER REVIEWED**

Average Daily Intake:

AIR INTAKE: (assume air concn of 0.2-2.7 ppb)(2-6); 17-235 ug; WATER INTAKE: (assume water concn of 0-4 ppb(1)) 0-8 ug; FOOD INTAKE: insufficient data(SRC).
[(1) Konasewich D et al; Status Report on Organic and Heavy Metal Contaminants in the Lake Erie, Michigan, Huron and Superior Basins. Great Lakes Quality Review Board (1978) (2) Arnts RR, Meeks SA; Biogenic Hydrocarbon Contribution to the Ambient Air of Selected Areas p. 31 USEPA-600/3-80-023 (1980) (3) Atshuller AP et al; Environ Sci Technol 5: 1009-16 (1981) (4) Lonneman WA et al; Environ Sci Technol 2: 1017-20 (1968) (5) Singh HB et al; Atmos Environ 15: 601-12 (1981) (6) Singh HB et al; Atmospheric Measurements of Selected Toxic Organic Chemicals USEPA-600/3-80-072 (1980)]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Toxicity Summary:

The acute toxicity of ethylbenzene to algae, aquatic invertebrates and fish is moderate. ... No information is available regarding chronic exposure of aquatic organisms to ethylbenzene. There is limited information regarding the toxicity of ethylbenzene to bacteria ... There are no data for terrestrial plants, birds, or wild mammals. Human exposure to ethylbenzene occurs mainly by inhalation; 40-60% of inhaled ethylbenzene is retained in the lung. Ethylbenzene is extensively metabolized, mainly to mandelic and phenylglyoxylic acids. These urinary metabolites can be used to monitor human exposures. Ethylbenzene has low acute and chronic toxicity for both animals and humans. It is toxic to the central nervous system and is an irritant of mucous membranes and the eyes. ... Ethylbenzene is an inducer of liver microsomal enzymes. It is not mutagenic or teratogenic ... No information is available on reproductive toxicity or carcinogenicity of ethylbenzene. A guidance value of 22 mg/ cu m (5 ppm) has been calculated from animal studies. /This value would correspond to a weekly absorbed dose (daily ventilation of 20 cu m with 60% retention) of about 2000 mg./ The estimated exposure of the general population (even in the worst case situation) is below this guidance value. Long term occupational exposure to ethylbenzene concentrations estimated to be of this order of magnitude did not cause adverse health effects in workers.
[Environmental Health Criteria 186: Ethylbenzene pp. 19-20 (1996) by the International Programme on Chemical Safety (IPCS) under the joint sponsorship of the United Nations Environment Programme, the International Labour Organisation and the World Health Organization.]**QC REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Evidence for Carcinogenicity:

CLASSIFICATION: D; not classifiable as to human carcinogenicity. BASIS FOR CLASSIFICATION: nonclassifiable due to lack of animal bioassays and human studies. HUMAN CARCINOGENICITY DATA: None. ANIMAL CARCINOGENICITY DATA: None.
[U.S. Environmental Protection Agency's Integrated Risk Information System (IRIS) on Ethylbenzene (100-41-4) Available from: http://www.epa.gov/ngispgm3/iris on the Substance File List as of March 15, 2000]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

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PROLONGED EXPOSURE TO ... VAPORS MAY RESULT IN FUNCTIONAL DISORDERS, INCREASE IN DEEP REFLEXES, IRRITATION OF UPPER RESPIRATORY TRACT, HEMATOLOGICAL DISORDERS (LEUKOPENIA AND LYMPHOCYTOSIS, IN PARTICULAR) AND ... HEPATOBILIARY COMPLAINTS.
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 2114]**PEER REVIEWED**

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[Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965. 92]**PEER REVIEWED**

Produces an irritant effect from chronic inhalation at 100 ppm (0.492 mg/L)/8 hr. /From table/
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[Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986. 413]**PEER REVIEWED**

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[American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices. 5th ed. Cincinnati, OH:American Conference of Governmental Industrial Hygienists, 1986. 244]**PEER REVIEWED**

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[Cleland, J.G., G.L. Kingsbury. Multimedia Environmental Goals for Environmental Assessment. Volume 1. EPA-600/7-77-136a. Research Triangle Park, NC: EPA, Nov. 1977.,p. E-148]**PEER REVIEWED**

EXPOSURE TO CONCN OF 5000 PPM /24.6 MG/L/ ... CAUSES INTOLERABLE IRRITATION OF EYES, MUCOUS MEMBRANES & NOSE.
[Patty, F. (ed.). Industrial Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New York: Interscience Publishers, 1963. 1232]**PEER REVIEWED**

HAZARD WARNING: ... exposure to 21.5 g/cu m (5000 ppm) ethylbenzene for a few seconds gives intolerable irritation of nose, eyes, and throat.
[Environmental Health Criteria 186: Ethylbenzene pp. 67 (1996) by the International Programme on Chemical Safety (IPCS) under the joint sponsorship of the United Nations Environment Programme, the International Labour Organisation and the World Health Organization.]**QC REVIEWED**

ETHYLBENZENE

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Medical Surveillance:

... EMPLOYMENT EXAMINATION SHOULD ENSURE THAT PERSONS WITH LIVER, KIDNEY, NERVOUS SYSTEM, BLOOD AND HEMOPOIETIC-ORGAN DISORDERS ARE /PROTECTED FROM EXPOSURE/ ... WOMEN WITH OVULATION AND MENSTRUAL CYCLE DISORDERS SHOULD ALSO BE /PROTECTED/.
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 2114]**PEER REVIEWED**

Consider the points of attack (eyes, upper respiratory system, skin, central nervous system) in placement and periodic physical examinations.
[Sittig, M. Handbook of Toxic and Hazardous Chemicals and Carcinogens, 1985. 2nd ed. Park Ridge, NJ: Noyes Data Corporation, 1985. 413]**PEER REVIEWED**

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Populations at Special Risk:

IN PERSONS WITH IMPAIRED PULMONARY FUNCTION, ESP THOSE WITH OBSTRUCTIVE AIRWAY DISEASES, BREATHING ETHYL BENZENE MIGHT CAUSE EXACERBATION OF SYMPTOMS DUE TO ITS IRRITANT PROPERTIES OR PSYCHIC REFLEX BRONCHOSPASM.
[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) PublicationNo. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981.]**PEER REVIEWED**

PERSONS WITH ... EXISTING SKIN DISORDERS MAY BE MORE SUSCEPTIBLE TO EFFECTS. ...
[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) PublicationNo. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981.]**PEER REVIEWED**

... PERSONS WITH LIVER, KIDNEY, NERVOUS SYSTEM, BLOOD AND HEMOPOIETIC-ORGAN DISORDERS. ... WOMEN WITH OVULATION AND MENSTRUAL CYCLE DISORDERS. ...
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Probable Routes of Human Exposure:

NIOSH (NOES Survey 1981-1983) has statistically estimated that 80,726 workers (21,785 of these are female) are potentially exposed to ethylbenzene in the US(1). Occupational exposure to ethylbenzene may occur via inhalation at municipal waste composting facilities where the air concn was found to be 78,000-178,000 ug/cu m(2),and through inhalation and dermal contact with this compound at worplaces where ethylbenzene is produced or used(SRC). The general population may be exposed to ethylbenzene via inhalation of ambient air, ingestion of foods and fish, and drinking contaminated water, and dermal contact with this compound and other products such as gasoline which contains ethylbenzene(SRC).
[(1) NIOSH; National Occupational Exposure Survey (NOES) (1983) (2) Eitzer BD; Environ Sci Technol 29: 896-902 (1995)]**PEER REVIEWED**

ETHYLBENZENE

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Body Burden:

Ethylbenzene was detected, not quantified, in 8 of 8 samples of mother's milk from 4 US urban areas(1). 16.5% of 387 expired air samples taken from 54 normal, healthy, urban volunteers were positive for ethylbenzene concn with an avg of 1.8 ng/l expired air(2). Whole blood samples from 250 subjects ranged in ethylbenzene concns from not detected to 59 ppb, with an avg of 1.0 ppb(3).
[(1) Pellizzari ED et al; Bull Environ Contam Toxicol 28: 322-8 (1982) (2) Krotoszynski BK et al; J Anal Toxicol 3: 225-34 (1979) (3) Antoine SR et al; Bull Environ Contam Toxicol 36: 364-71 (1986)]**PEER REVIEWED**

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Average Daily Intake:

AIR INTAKE: (assume air concn of 0.2-2.7 ppb)(2-6); 17-235 ug; WATER INTAKE: (assume water concn of 0-4 ppb(1)) 0-8 ug; FOOD INTAKE: insufficient data(SRC).

[(1) Konasewich D et al; Status Report on Organic and Heavy Metal Contaminants in the Lake Erie, Michigan, Huron and Superior Basins. Great Lakes Quality Review Board (1978) (2) Arnts RR, Meeks SA; Biogenic Hydrocarbon Contribution to the Ambient Air of Selected Areas p. 31 USEPA-600/3-80-023 (1980) (3) Atshuller AP et al; Environ Sci Technol 5: 1009-16 (1981) (4) Lonneman WA et al; Environ Sci Technol 2: 1017-20 (1968) (5) Singh HB et al; Atmos Environ 15: 601-12 (1981) (6) Singh HB et al; Atmospheric Measurements of Selected Toxic Organic Chemicals USEPA-600/3-80-072 (1980)]**PEER REVIEWED**

ETHYLBENZENE

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Emergency Medical Treatment:

Emergency Medical Treatment:

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The following Overview, *** ETHYLBENZENE ***, is relevant for this HSDB record chemical.

Life Support:

- This overview assumes that basic life support measures have been instituted.

Clinical Effects:

SUMMARY OF EXPOSURE

0.2.1.1 ACUTE EXPOSURE

- Ethylbenzene is an eye, skin, and mucous membrane irritant. Narcosis may also occur.
- Exposure to ethylbenzene at significant concentrations may cause profuse lacrimation, conjunctivitis, nasal and respiratory tract irritation, chest constriction, vertigo, headache, irritability, and possibly functional nervous system disturbances at high concentrations.
- Chronic exposure in humans may caused fatigue, sleepiness, headache, and irritation of the eyes and respiratory tract.
- In experimental animals, exposure to ethylbenzene may cause eye, skin, and mucous membrane irritation; changes in liver and kidney weights; CNS depression; pulmonary edema; and respiratory failure.

HEENT

0.2.4.1 ACUTE EXPOSURE

- Ethylbenzene can be an eye irritant.

RESPIRATORY

0.2.6.1 ACUTE EXPOSURE

- Ethyl benzene is a respiratory tract irritant and is a

pulmonary aspiration hazard following large ingestions. In fatal cases, pulmonary edema had developed; death occurs in respiratory failure. However, human studies demonstrated no signs or symptoms of respiratory tract irritation at 85 and 100 ppm.

NEUROLOGIC

0.2.7.1 ACUTE EXPOSURE

- Ethyl benzene has CNS depressant (narcotic) properties at high concentrations.
- CNS symptoms may include headache, nausea, weakness, incoordination, dizziness, sleepiness, loss of coordination, judgement, and consciousness, and coma or death may occur with significant exposure. Cerebral edema may occur in fatal poisonings.

GASTROINTESTINAL

0.2.8.1 ACUTE EXPOSURE

- Ethyl benzene is a pulmonary aspiration hazard following ingestion, and is toxic with ingestion exposure. Ingestion would be predicted to cause GI tract irritation or burns.

HEPATIC

0.2.9.1 ACUTE EXPOSURE

- Slight changes in the liver occurred in rats exposed to 600 ppm for up to 16 weeks.

GENITOURINARY

0.2.10.1 ACUTE EXPOSURE

- Slight changes in the kidneys occurred in rats exposed to 600 ppm for up to 16 weeks.

HEMATOLOGIC

0.2.13.1 ACUTE EXPOSURE

- Ethyl benzene has been shown NOT to have the myelotoxic activity associated with BENZENE.

DERMATOLOGIC

0.2.14.1 ACUTE EXPOSURE

- Dermal contact causes inflammation and erythema. Ethyl benzene can be absorbed through intact skin.

REPRODUCTIVE HAZARDS

- Ethyl benzene is teratogenic and fetotoxic in experimental animals, and has been detected in umbilical cord blood.

Laboratory:

- Urinary levels of mandelic acid can be used as an indicator of exposure to ethylbenzene.

Treatment Overview:

SUMMARY EXPOSURE

- FIRST AID (NIOSH, 2000) -
  1. EYE EXPOSURE - Immediately wash the eyes with large amounts of water, occasionally lifting the lower and upper lids. Get medical attention immediately. Contact lenses should not be worn when working with this chemical.
  2. DERMAL EXPOSURE - Flush the contaminated skin with water promptly. If this chemical penetrates the clothing, immediately remove the clothing and flush the skin with water promptly. If irritation persists after washing, get medical attention.
  3. INHALATION EXPOSURE - Move the exposed person to fresh air at once. If breathing has stopped, perform mouth-to-mouth resuscitation. Keep the affected person warm and at rest. Get medical attention as soon as possible.
  4. ORAL EXPOSURE - If this chemical has been swallowed, get medical attention immediately.
  5. TARGET ORGANS - Eyes, skin, respiratory tract, and central nervous system.
- GENERAL -
  1. Move victims of inhalation exposure from the toxic environment and administer 100% humidified supplemental oxygen with assisted ventilation as required. Exposed skin and eyes should be copiously flushed with water. Because of the potential for rapid onset of CNS depression or seizures with possible aspiration of gastric contents, EMESIS SHOULD NOT BE INDUCED. Cautious gastric lavage followed by administration of activated charcoal may be of benefit if the patient is seen soon after the exposure.
- INHALATION EXPOSURE -
  1. DECONTAMINATION: Move patient to fresh air. Monitor for respiratory distress. If cough or difficulty in breathing develops, evaluate for respiratory tract irritation, bronchitis, or pneumonitis. Administer 100 percent humidified supplemental oxygen with assisted ventilation as required.
  2. If bronchospasm and wheezing occur, consider treatment with inhaled sympathomimetic agents.
  3. PULMONARY EDEMA (NONCARDIOGENIC): Maintain ventilation and oxygenation and evaluate with frequent arterial blood gas or pulse oximetry monitoring. Early use of

PEEP and mechanical ventilation may be needed.

- DERMAL EXPOSURE -
  1. DECONTAMINATION: Wash exposed area extremely thoroughly with soap and water. A physician may need to examine the area if irritation or pain persists.
  2. Treat dermal irritation or burns with standard topical therapy. Patients developing dermal hypersensitivity reactions may require treatment with systemic or topical corticosteroids or antihistamines.
  3. Some chemicals can produce systemic poisoning by absorption through intact skin. Carefully observe patients with dermal exposure for the development of any systemic signs or symptoms and administer symptomatic treatment as necessary.
- EYE EXPOSURE -
  1. DECONTAMINATION: Exposed eyes should be irrigated with copious amounts of tepid water for at least 15 minutes. If irritation, pain, swelling, lacrimation, or photophobia persist, the patient should be seen in a health care facility.
- ORAL EXPOSURE -
  1. Because of the potential for CNS depression or gastrointestinal tract irritation, do not induce emesis.
  2. Weigh the potential toxicity of the amount of ethylbenzene ingested against the substantial risk of pulmonary aspiration of gastric contents. Ethylbenzene may "wick" up around a lavage tube, allowing pulmonary aspiration.
     a. Significant esophageal or gastrointestinal tract irritation or burns may occur following ingestion. The possible benefit of early removal of some ingested material by cautious gastric lavage must be weighed against potential complications of bleeding or perforation.
  3. GASTRIC LAVAGE: Consider after ingestion of a potentially life-threatening amount of poison if it can be performed soon after ingestion (generally within 1 hour). Protect airway by placement in Trendelenburg and left lateral decubitus position or by endotracheal intubation. Control any seizures first.
     a. CONTRAINDICATIONS: Loss of airway protective reflexes or decreased level of consciousness in unintubated patients; following ingestion of corrosives; hydrocarbons (high aspiration potential); patients at risk of hemorrhage or gastrointestinal perforation;

and trivial or non-toxic ingestion.

4. ACTIVATED CHARCOAL/CATHARTIC: Administer charcoal slurry, aqueous or mixed with saline cathartic or sorbitol. The FDA suggests 240 mL of diluent/30 g of charcoal. Usual charcoal dose is 25 to 100 grams in adults and adolescents, 25 to 50 grams in children (1 to 12 years old), and 1 gram/kilogram in infants less than 1 year old.
   a. Routine use of cathartics is NOT recommended. If used, administer only ONE dose of cathartic. Administer one dose of a cathartic, mixed with charcoal or given separately. See "Treatment: Prevention of Absorption" in the main document.
5. Observe patients with ingestion carefully for the possible development of esophageal or gastrointestinal tract irritation or burns. If signs or symptoms of esophageal irritation or burns are present, consider endoscopy to determine the extent of injury.

ORAL EXPOSURE

- Because of the potential for CNS depression or gastrointestinal tract irritation, Do NOT induce emesis.
- Weigh the potential toxicity of the amount of ethylbenzene ingested against the substantial risk of aspiration. Ethylbenzene may "wick" up around a lavage tube, allowing pulmonary aspiration.
  1. Significant esophageal or gastrointestinal tract irritation or burns may occur following ingestion. The possible benefit of early removal of some ingested material by cautious gastric lavage must be weighed against potential complications of bleeding or perforation.
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INHALATION EXPOSURE

- DECONTAMINATION: Move patient to fresh air. Monitor for respiratory distress. If cough or difficulty in breathing develops, evaluate for respiratory tract irritation, bronchitis, or pneumonitis. Administer 100 percent humidified supplemental oxygen with assisted ventilation as required.
- If bronchospasm and wheezing occur, consider treatment with inhaled sympathomimetic agents.
- PULMONARY EDEMA (NONCARDIOGENIC): Maintain ventilation and oxygenation and evaluate with frequent arterial blood gas or pulse oximetry monitoring. Early use of PEEP and mechanical ventilation may be needed.

EYE EXPOSURE

- DECONTAMINATION: Exposed eyes should be irrigated with copious amounts of tepid water for at least 15 minutes. If irritation, pain, swelling, lacrimation, or photophobia persist, the patient should be seen in a health care facility.

DERMAL EXPOSURE

- DECONTAMINATION: Wash exposed area extremely thoroughly with soap and water. A physician may need to examine the area if irritation or pain persists.
- Treat dermal irritation or burns with standard topical therapy. Patients developing dermal hypersensitivity reactions may require treatment with systemic or topical corticosteroids or antihistamines.
- Some chemicals can produce systemic poisoning by absorption through intact skin. Carefully observe patients with dermal exposure for the development of any systemic signs or symptoms and administer symptomatic treatment as necessary.

[Rumack BH: POISINDEX(R) Information System. Micromedex, Inc., Englewood, CO, 2001; CCIS Volume 107, edition exp February, 2001. Hall AH & Rumack BH (Eds):TOMES(R) Information System. Micromedex, Inc., Englewood, CO, 2001; CCIS Volume 107, edition exp February, 2001.] **PEER REVIEWED**

Antidote and Emergency Treatment:

Basic treatment: Establish a patent airway. Suction if necessary. Watch for signs of respiratory insufficiency and assist ventilations if necessary. Administer oxygen by nonrebreather mask at 10 to 15 L/min. Monitor for pulmonary edema and treat if necessary ... . Monitor for shock and treat if necessary ... . For eye contamination, flush eyes immediately with water. Irrigate each eye continuously with normal saline during transport ... . Do not use emetics. For ingestion, rinse mouth and administer 5 ml/kg up to 200 ml of water for dilution if the patient can swallow, has a strong gag reflex, and does not drool. Administer activated charcoal ... . /Aromatic hydrocarbons and related compounds/
[Bronstein, A.C., P.L. Currance; Emergency Care for Hazardous Materials Exposure. 2nd ed. St. Louis, MO. Mosby Lifeline. 1994.,p. 181-2]**PEER REVIEWED**

Advanced treatment: Consider orotracheal or nasotracheal intubation for airway control in the patient who is unconscious or in respiratory arrest. Positive-pressure ventilation techniques with a bag-valve-mask device may be beneficial. Monitor cardiac rhythm and treat arrhythmias if necessary ... . Start an IV with D5W /SRP: "To keep open", minimal flow rate/. Use lactated Ringer's if signs of hypovolemia are present. Watch for signs of fluid overload. Consider drug therapy for pulmonary edema ... . Treat seizures with diazepam (Valium) ... . Use proparacaine hydrochloride to assist eye irrigation ... . /Aromatics hydrocarbons and related compounds/
[Bronstein, A.C., P.L. Currance; Emergency Care for Hazardous Materials Exposure. 2nd ed. St. Louis, MO. Mosby Lifeline. 1994. 182]**PEER REVIEWED**

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Emergency Medical Treatment:

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Life Support:

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Clinical Effects:

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- Ethylbenzene is an eye, skin, and mucous membrane irritant. Narcosis may also occur.
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HEENT

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GASTROINTESTINAL

0.2.8.1 ACUTE EXPOSURE

- Ethyl benzene is a pulmonary aspiration hazard following ingestion, and is toxic with ingestion exposure. Ingestion would be predicted to cause GI tract irritation or burns.

HEPATIC

0.2.9.1 ACUTE EXPOSURE

- Slight changes in the liver occurred in rats exposed to 600 ppm for up to 16 weeks.

GENITOURINARY

0.2.10.1 ACUTE EXPOSURE

- Slight changes in the kidneys occurred in rats exposed to 600 ppm for up to 16 weeks.

HEMATOLOGIC

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  3. INHALATION EXPOSURE - Move the exposed person to fresh air at once. If breathing has stopped, perform mouth-to-mouth resuscitation. Keep the affected person warm and at rest. Get medical attention as soon as possible.
  4. ORAL EXPOSURE - If this chemical has been swallowed, get medical attention immediately.
  5. TARGET ORGANS - Eyes, skin, respiratory tract, and central nervous system.
- GENERAL -
  1. Move victims of inhalation exposure from the toxic environment and administer 100% humidified supplemental oxygen with assisted ventilation as required. Exposed skin and eyes should be copiously flushed with water. Because of the potential for rapid onset of CNS depression or seizures with possible aspiration of gastric contents, EMESIS SHOULD NOT BE INDUCED. Cautious gastric lavage followed by administration of activated charcoal may be of benefit if the patient is seen soon after the exposure.
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     a. CONTRAINDICATIONS: Loss of airway protective reflexes or decreased level of consciousness in unintubated patients; following ingestion of corrosives; hydrocarbons (high aspiration potential); patients at risk of hemorrhage or gastrointestinal perforation;

and trivial or non-toxic ingestion.

4. ACTIVATED CHARCOAL/CATHARTIC: Administer charcoal slurry, aqueous or mixed with saline cathartic or sorbitol. The FDA suggests 240 mL of diluent/30 g of charcoal. Usual charcoal dose is 25 to 100 grams in adults and adolescents, 25 to 50 grams in children (1 to 12 years old), and 1 gram/kilogram in infants less than 1 year old.
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ORAL EXPOSURE

- Because of the potential for CNS depression or gastrointestinal tract irritation, Do NOT induce emesis.
- Weigh the potential toxicity of the amount of ethylbenzene ingested against the substantial risk of aspiration. Ethylbenzene may "wick" up around a lavage tube, allowing pulmonary aspiration.

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INHALATION EXPOSURE

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EYE EXPOSURE

- DECONTAMINATION: Exposed eyes should be irrigated with copious amounts of tepid water for at least 15 minutes. If irritation, pain, swelling, lacrimation, or photophobia persist, the patient should be seen in a health care facility.

DERMAL EXPOSURE

- DECONTAMINATION: Wash exposed area extremely thoroughly with soap and water. A physician may need to examine the area if irritation or pain persists.
- Treat dermal irritation or burns with standard topical therapy. Patients developing dermal hypersensitivity reactions may require treatment with systemic or topical corticosteroids or antihistamines.
- Some chemicals can produce systemic poisoning by absorption through intact skin. Carefully observe patients with dermal exposure for the development of any systemic signs or symptoms and administer symptomatic treatment as necessary.

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PEER REVIEWED

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Antidote and Emergency Treatment:

Basic treatment: Establish a patent airway. Suction if necessary. Watch for signs of respiratory insufficiency and assist ventilations if necessary. Administer oxygen by nonrebreather mask at 10 to 15 L/min. Monitor for pulmonary edema and treat if necessary ... . Monitor for shock and treat if necessary ... . For eye contamination, flush eyes immediately with water. Irrigate each eye continuously with normal saline during transport ... . Do not use emetics. For ingestion, rinse mouth and administer 5 ml/kg up to 200 ml of water for dilution if the patient can swallow, has a strong gag reflex, and does not drool. Administer activated charcoal ... . /Aromatic hydrocarbons and related compounds/

[Bronstein, A.C., P.L. Currance; Emergency Care for Hazardous Materials Exposure. 2nd ed. St. Louis, MO. Mosby Lifeline. 1994.,p. 181-2]**PEER REVIEWED**

Advanced treatment: Consider orotracheal or nasotracheal intubation for airway control in the patient who is unconscious or in respiratory arrest. Positive-pressure ventilation techniques with a bag-valve-mask device may be beneficial. Monitor cardiac rhythm and treat arrhythmias if necessary ... . Start an IV with D5W /SRP: "To keep open", minimal flow rate/. Use lactated Ringer's if signs of hypovolemia are present. Watch for signs of fluid overload. Consider drug therapy for pulmonary edema ... . Treat seizures with diazepam (Valium) ... . Use proparacaine hydrochloride to assist eye irrigation ... . /Aromatics hydrocarbons and related compounds/

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Animal Toxicity Studies:

Toxicity Summary:

The acute toxicity of ethylbenzene to algae, aquatic invertebrates and fish is moderate. ... No information is available regarding chronic exposure of aquatic organisms to ethylbenzene. There is limited information regarding the toxicity of ethylbenzene to bacteria ... There are no data for terrestrial plants, birds, or wild mammals. Human exposure to ethylbenzene occurs mainly by inhalation; 40-60% of inhaled ethylbenzene is retained in the lung. Ethylbenzene is extensively metabolized, mainly to mandelic and phenylglyoxylic acids. These urinary metabolites can be used to monitor human exposures. Ethylbenzene has low acute and chronic toxicity for both animals and humans. It is toxic to the central nervous system and is an irritant of mucous membranes and the eyes. ... Ethylbenzene is an inducer of liver microsomal enzymes. It is not mutagenic or teratogenic ... No information is available on reproductive toxicity or carcinogenicity of ethylbenzene. A guidance value of 22 mg/ cu m (5 ppm) has been calculated from animal studies. /This value would correspond to a weekly absorbed dose (daily ventilation of 20 cu m with 60% retention) of about 2000 mg./ The estimated exposure of the general population (even in the worst case situation) is below this guidance value. Long term occupational exposure to ethylbenzene concentrations estimated to be of this order of magnitude did not cause adverse health effects in workers.
[Environmental Health Criteria 186: Ethylbenzene pp. 19-20 (1996) by the International Programme on Chemical Safety (IPCS) under the joint sponsorship of the United Nations Environment Programme, the International Labour Organisation and the World Health Organization.]**QC REVIEWED**

Evidence for Carcinogenicity:

CLASSIFICATION: D; not classifiable as to human carcinogenicity. BASIS FOR CLASSIFICATION: nonclassifiable due to lack of animal bioassays and human studies. HUMAN CARCINOGENICITY DATA: None. ANIMAL CARCINOGENICITY DATA: None.
[U.S. Environmental Protection Agency's Integrated Risk Information System (IRIS) on Ethylbenzene (100-41-4) Available from: http://www.epa.gov/ngispgm3/iris on the Substance File List as of March 15, 2000]**PEER REVIEWED**

Non-Human Toxicity Excerpts:

... From ingestion of or exposure of skin or lung to high concns causes /CNS depression/ in animals. Although similar to benzene, ethylbenzene apparently does not cause bone marrow problems.
[Friberg, L., Nordberg, G.F., Kessler, E. and Vouk, V.B. (eds). Handbook of the Toxicology of Metals. 2nd ed. Vols I, II.: Amsterdam: Elsevier Science Publishers B.V., 1986. 288]**PEER REVIEWED**

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[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 2114]**PEER REVIEWED**

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IN GUINEA PIGS, 0.3% BY VOL IS MAX AMT FOR 1 HR WITHOUT SERIOUS SYMPTOMS; 0.1% BY VOL IS MAX AMT FOR SEVERAL HR WITHOUT SERIOUS DISTURBANCES. /FROM TABLE/
[Patty, F. (ed.). Industrial Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New York: Interscience Publishers, 1963. 1232]**PEER REVIEWED**

REPEATED APPLICATIONS OF UNDILUTED ETHYLBENZENE TO THE SKIN OF RABBITS CAUSED ... BLISTERING.
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... RATS, RABBITS, GUINEA PIGS, AND MONKEYS /WERE EXPOSED/ TO CONCN OF ... 400-2200 PPM, 7 TO 8 HR/DAY, 5 DAYS A WK FOR AS LONG AS 6 MONTHS. THE GUINEA PIGS, RABBITS, AND MONKEYS WERE NOT AFFECTED ... SLIGHT INCREASE IN AVG WT OF KIDNEYS AND LIVERS WERE OBSERVED IN RATS EXPOSED TO 400 PPM FOR 186 DAYS.
[Patty, F. (ed.). Industrial Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New York: Interscience Publishers, 1963. 1232]**PEER REVIEWED**

... RATS /WERE INJECTED/ SUBCUTANEOUSLY WITH 1 ML ... PER KG OF BODY WT DAILY FOR 2 WEEKS AND ... NO DECREASE IN THE TOTAL FEMORAL MARROW NUCLEATED CELL COUNT /WAS OBSERVED/. THESE ANIMALS DEVELOPED A LEUCOCYTOSIS INSTEAD OF SEVERE LEUCOPENIAS FOUND IN BENZENE-DOSED ANIMALS WHICH SERVED AS POSITIVE CONTROLS.

[Patty, F. (ed.). Industrial Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New York: Interscience Publishers, 1963. 1232]**PEER REVIEWED**

EXPOSURE TO 2000 PPM FOR UP TO 375 MIN CAUSED IN SOME OF /GUINEA PIGS/ ... MOTOR ATAXIA AND APPARENT UNCONSCIOUSNESS; WITH 10,000 PPM THIS STAGE WAS REACHED IN 18 MIN. IT WAS PRECEDED BY VERTIGO, UNSTEADINESS AND ATAXIA.
[Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965. 92]**PEER REVIEWED**

LIVER & KIDNEY WT INCREASED IN RATS GIVEN SUBCHRONIC ORAL DOSES OF 408-680 MG/KG/DAY FOR 182 DAYS. /FROM TABLE/
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1345]**PEER REVIEWED**

INHALATION @ 3050 PPM (15 MG/L) PRODUCED LOSS OF RIGHTING RESPONSE IN MICE & DEATH IN 2 HR FROM 9150 PPM (45 MG/L). IN GUINEA PIGS 1000 PPM (4.92 MG/L)/3 MIN PRODUCED SLIGHT NASAL IRRITATION, @ 8 MIN EYE IRRITATION; 2000 PPM (9.84 MG/L)/1 MIN PRODUCED MODERATE EYE & NASAL IRRITATION, UNCONSCIOUSNESS @ 345 MIN. /FROM TABLE/
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1344]**PEER REVIEWED**

SUBACUTE EXPOSURE OF MALE RATS TO 2000 PPM PRODUCED INCREASES OF DOPAMINE & NORADRENALINE LEVELS & TURNOVER IN VARIOUS PARTS OF HYPOTHALAMUS & MEDIAN EMINENCE 16-18 HR FOLLOWING LAST EXPOSURE.
[ANDERSON K ET AL, TOXICOL APPL PHARMACOL 60 (3): 535 (1981)]**PEER REVIEWED**

Rats inhaling 600, 1200, or 2400 mg ethylbenzene/cu m for 24 hr/day from days 7-15 of pregnancy showed mild toxicity. The highest dose retarded skeletal development and weight gain in the fetuses and increased the incidence of extra ribs. Sacral displacement with abnormal development was observed in 2 instances. Thus, ethylbenzene, has some embryotoxic and teratogenic activity.
[Tatrai E et al; Egeszsegtudomany 26 (3): 297-303 (1982)]**PEER REVIEWED**

Ethylbenzene was investigated ... as a sensory irritant in mice. The concn necessary to depress the respiratory rate by 50% (RD 50) due to sensory irritation of the upper respiratory tract was 4060 ppm. ... A model for the sensory irritating action ... was proposed on the basis of ... physical interaction with a receptor protein.
[Nielsen GD, Alarie Y; Toxical Appl Pharmacol 65 (3): 459-77 (1982)]**PEER REVIEWED**

Drop application to rabbit eyes caused slight irritation and no corneal injury demonstrable by fluorescein staining. Standard testing on rabbit eyes gave an injury grade of 2 on a scale of 10.
[Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles

C. Thomas Publisher, 1986. 413]**PEER REVIEWED**

Rats were exposed for 3 days by inhalation to 2000 ppm of a xylene mixture, or ... ethylbenzene. All solvents increased hepatic cytochrome p450 concn and NADPH-cytochrome C reductase activity. The ability of ethylbenzene to modify the metabolism of other potentially toxic substances in liver, kidney, and lung microsomes suggested the possibility of synergistic toxic responses.
[Toftgard R, Nilsen OG; Toxicol 23 (2-3): 197-212 (1982)]**PEER REVIEWED**

Concn of < 0.25 mg/l can cause tainting of fish flesh.
[Cleland, J.G., G.L. Kingsbury. Multimedia Environmental Goals for Environmental Assessment. Volume 1. EPA-600/7-77-136a. Research Triangle Park, NC: EPA, Nov. 1977.,p. E-148]**PEER REVIEWED**

Neither maternal toxicity nor embryotoxicity was observed in gravid rabbits exposed to ethylbenzene /by inhalation/ at 100 or 1000 ppm.
[NIOSH; Teratologic Assessment of Ethylbenzene and 2-Ethoxyethanol p.iii (1981) NIOSH Contract No. 210-79-0037]**PEER REVIEWED**

Neither maternal toxicity nor embyrotoxicity was observed /in pregnant rats/ exposed to ethylbenzene /by inhalation/ at 100 ppm ... but /1000 ppm/ induced some indications of toxicity. ... A significant increase in the incidence of extra ribs was detected in rat fetuses exposed in utero to the high level.
[NIOSH; Teratologic Assessment of Ethylbenzene and 2-Ethoxyethanol p.iii (1981) NIOSH Contract No. 210-79-0037]**PEER REVIEWED**

Mice, B6C3F1 Fischer-344 rats, and /rabbits /New Zealand/ (five/sex/group) were exposed by inhalation to ethylbenzene vapors for 6 hr/day, 5 days/week for 4 weeks (20 exposures). Rats and mice received 0, 99, 382, or 782 ppm ethylbenzene while rabbits received 0, 382, 782, or 1610 ppm. No changes were evident in mortality patterns, clinical chemistries, urinalyses, or treatment-related gross/microscopic (including ophthalmologic) lesions. Rats exhibited sporadic lacrimation and salivation, as well as significantly increased liver weights at 382 and 782 ppm, and small increases in leukocyte counts at 782 ppm. Males at this exposure level also showed marginal elevations in platelet counts. In mice, females showed statistically increased absolute and relative liver weights at 382 and 782 ppm while males had statistically increased relative liver-to-brain weight ratios only at 782 ppm. Female rabbits at the high exposure level of 1610 ppm gained weight more slowly than controls (not statistically significant); males showed a similar transient downward trend after 1 week, but showed no differences from controls at study's end. A no observed adverse effect level (NOAEL) of 382 ppm appears appropriate for rats and mice with a lowest observed adverse effect level (LOAEL) of 782 ppm. A NOAEL of 782 ppm and LOAEL of 1610 ppm are appropriate for rabbits.
[Cragg ST et al; Fundam Appl Toxicol 13 (3): 399-408 (1989)]**PEER REVIEWED**

Repeated application of undiluted ethyl benzene to the ear and shaved abdominal area of rabbits (10-20 applications over a period of 2-4 wk) resulted in erthyema, edema, and superficial necrosis. ... Two drops of ethyl benzene into the conjunctival sac produced only a slight irritation of the conjunctival membranes but no corneal injury.
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values and Biological Exposure

Indices. 6th ed. Volumes I,II, III. Cincinnati, OH: ACGIH, 1991. 581]**PEER REVIEWED**

Inhalation of 2600 mg/cu m (600 ppm) ethyl benzene 7 hr/day, 5 days/wk for 186 days caused degeneration of the germinal epithelium in the testes of rabbits and monkeys but not of rats. Pregnant rats exposed at 100 or 1000 ppm 6 hr/day for 3 wk prior to mating and on days 1-19 of gestation had pups with a significant increase ($p < 0.05$) in extra rib formation; at the higher dose, maternal toxicity was indicated by increased liver, kidney, and spleen weights.
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Volumes I,II, III. Cincinnati, OH: ACGIH, 1991. 582]**PEER REVIEWED**

... CONCLUSIONS: Under the conditions of these 2 yr inhalation studies, there was clear evidence of carcinogenic activity of ethylbenzene in male F344/N rats based on incr incidences of renal tubule neoplasms. The incidences of testicular adenoma were also incr. There was some evidence of carcinogenic activity of ethylbenzene in female F344/N rats based on incr incidences of renal tubule adenomas. There was some evidence of carcinogenic activity of ethylbenzene in male B6C3F1 mice based on incr incidences of alveolar/bronchiolar neoplasms. There was some evidence of carcinogenic activity of ethylbenzene in female B6C3F1 mice based on incr incidences of hepatocellular neoplasms.
[Toxicology & Carcinogenesis Studies of Ethylbenzene in F344/N Rats and B6C3F1 Mice p.5 Technical Report Series No. 466 (1999) NIH Publication No. 99-3956 U.S. Department of Health and Human Services, National Toxicology Program, National Institute of Environmental Health Sciences, Research Triangle Park, NC 27709]**PEER REVIEWED**

National Toxicology Program Studies:

... 2 Yr Study in Rats: Groups of 50 male and 50 female F344/N rats were exposed to 0, 75, 250 or 750 ppm ethylbenzene 6 hr day, 5 days/wk for 104 wk. ... 2 Yr Study in Mice: Groups of 50 male and 50 female B6C3F1 mice were exposed to 0, 75, 250 or 750 ppm ethylbenzene by inhalation, 6 hr/day, 5 days/wk for 103 wk. ... CONCLUSIONS: Under the conditions of these 2 yr inhalation studies, there was clear evidence of carcinogenic activity of ethylbenzene in male F344/N rats based on incr incidences of renal tubule neoplasms. The incidences of testicular adenoma were also incr. There was some evidence of carcinogenic activity of ethylbenzene in female F344/N rats based on incr incidences of renal tubule adenomas. There was some evidence of carcinogenic activity of ethylbenzene in male B6C3F1 mice based on incr incidences of alveolar/bronchiolar neoplasms. There was some evidence of carcinogenic activity of ethylbenzene in female B6C3F1 mice based on incr incidences of hepatocellular neoplasms.
[Toxicology & Carcinogenesis Studies of Ethylbenzene in F344/N Rats and B6C3F1 Mice p.5 Technical Report Series No. 466 (1999) NIH Publication No. 99-3956 U.S. Department of Health and Human Services, National Toxicology Program, National Institute of Environmental Health Sciences, Research Triangle Park, NC 27709]**QC REVIEWED**

Non-Human Toxicity Values:

LD50 Rat oral 5.46 g/kg.
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals,

Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 643]**PEER REVIEWED**

LD50 Rat oral 3500 mg/kg
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1522]**PEER REVIEWED**

LD50 Mouse ip 2272 mg/kg
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1522]**PEER REVIEWED**

LD50 Rabbit skin 17,800 mg/kg
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1522]**PEER REVIEWED**

Ecotoxicity Values:

LC50 Lepomis macrochirus 32 mg/l/96 hr /Conditions of bioassay not specified/
[Pickering QH, Henderson C; J Water Pollut Control Fed 38: 1419 (1966)]**PEER REVIEWED**

LC50 Carassius auratus 94.44 mg/l/96 hr /Conditions of bioassay not specified/
[Pickering QH, Henderson C; J Water Pollut Control Fed 38: 1419 (1966)]**PEER REVIEWED**

LC50 Lebistes reticulatus 97.10 mg/l/96 hr /Conditions of bioassay not specified/
[Pickering QH, Henderson C; J Water Pollut Control Fed 38: 1419 (1966)]**PEER REVIEWED**

LC50 Mysidopsis bahia (shrimp) 87.6 mg/l 96 hr in a static unmeasured bioassay
[USEPA; In-depth Studies on Health Environmental Impacts of Selected Water Pollutants (1978) EPA No 68-01-4646]**PEER REVIEWED**

LC50 Cyprinodon variegatus (sheepshead minnow) 275 mg/l 96 hr in a static unmeasured bioassay
[USEPA; In-depth Studies on Health Environmental Impacts of Selected Water Pollutants (1978) EPA No 68-01-4646]**PEER REVIEWED**

LC50 Pimephales promelas (fathead minnow) 42.3 (hardwater) to 48.5 (softwater) mg/l 96 hr /Conditions of bioassay not specified/
[Pickering OH, Henderson C; J Water Pollut Control Fed 38: 1419 (1966)]**PEER REVIEWED**

LC50 Poecilla reticulata (guppy) 97.1 mg/l/96 hr /Conditions of bioassay not specified/
[Pickering OH, Henderson C; J Water Pollut Control Fed 38: 1419 (1966)]**PEER REVIEWED**

Toxicity threshold (cell multiplication inhibition test): Microcystis aeruginosa (algae) 33 mg/l;

Scenedesmus quadricauda (green algae) > 160 mg/l
[Verschueren, K. Handbook of Environmental Data on Organic Chemicals. 3rd ed. New York, NY: Van Nostrand Reinhold Co., 1996. 946]**PEER REVIEWED**

Toxicity threshold (cell multiplication inhibition test): Entosiphon sulcatum (protozoa) 140 mg/l; Uronema parduczi Chatton-Lwoff (protozoa) > 110 mg/l.
[Verschueren, K. Handbook of Environmental Data on Organic Chemicals. 3rd ed. New York, NY: Van Nostrand Reinhold Co., 1996. 946]**PEER REVIEWED**

Toxicity threshold (cell multiplication inhibition test): Pseudomonas putida (bacteria) 12 mg/l.
[Verschueren, K. Handbook of Environmental Data on Organic Chemicals. 3rd ed. New York, NY: Van Nostrand Reinhold Co., 1996. 946]**PEER REVIEWED**

LC50 Palaemonetes pugio (grass shrimp, adult) 14,400 ug/l/24 hr in a static unmeasured bioassay
[USEPA; Ambient Water Quality Criteria Doc: Ethylbenzene p.3-7 (1980) EPA 440/5-80-048]**PEER REVIEWED**

LC50 Palaemonetes pugio (grass shrimp, larva) 10,200 ug/l/24 hr in a static unmeasured bioassay
[USEPA; Ambient Water Quality Criteria Doc: Ethylbenzene p.3-7 (1980) EPA 440/5-80-048]**PEER REVIEWED**

LC50 Pimephales promelas (fathead minnow) 12.1 mg/l/96 hr (confidence limit 11.5 - 12.7 mg/l), flow-through bioassay with measured concentrations, 26.1 deg C, dissolved oxygen 7.0 mg/l, hardness 45.6 mg/l calcium carbonate, alkalinity 43.0 mg/l calcium carbonate, and pH 7.39.
[Geiger D.L., Poirier S.H., Brooke L.T., Call D.J., eds. Acute Toxicities of Organic Chemicals to Fathead Minnows (Pimephales Promelas). Vol. III. Superior,Wisconsin: University of Wisconsin-Superior, 1986. 189]**PEER REVIEWED**

TSCA Test Submissions:

In a single generation reproduction study, 380 female and 60 male Wistar rats were exposed to ethylbenzene at average daily concentrations of 97 or 959 ppm 7 hours per day, 5 days per week for 3 weeks. They were then mated and exposed daily on gestation days (GD) 1-19 at concentrations of 96 (low) or 985 (high) ppm. Animals were sacrificed and examined on GD 21. No significant differences were observed between treatment groups and controls in food consumption, gestational body weights (of pregnant rats), organ weights (of male rats), histopathology of liver, kidney or lungs, percent pregnancy, no. of corpora lutea, no. of implants, total live or dead fetuses, no. of live or dead fetuses per litter, no. of resorptions per litter and percent litters with resorptions. A significant difference (ANOVA, Duncan's multiple range test) was observed in pregestational body weights in both treatment groups. Maternal toxicity was indicated in the high dose groups (dosed at the high level during both periods or dosed with air during pregestational and with the high level during gestation) by significant differences (ANOVA, Duncan's multiple range test) in liver, spleen and kidney weights. Statistically significant differences were seen in mean crown-rump length (in the group which was dosed at the high level during both periods), supernumerary ribs (in the 2 high dose groups and the group which was dosed with air

pregestationally and with the low level during gestation) and rudimentary rib incidence (in the group dosed with air during pregestation and with the high level during gestation).
[Battelle Pacific Northwest Laboratories; Teratologic Assessment of Ethylbenzene and 2-Ethoxyethanol with Cover Letter Dated 061887, (1981), EPA Document No. 86870000402, Fiche No. OTS0513150]
UNREVIEWED

In a single generation reproduction study 96 New Zealand White rabbits were artifically inseminated and exposed to ethylbenzene at average daily concentrations of 99 or 962 ppm 7 hours per day, through gestation day (GD) 24. Animals were sacrificed and examined on GD 30. Mortality was observed in 2 does, 1 from each dose group. No significant differences were observed between treatment groups and controls in the following: food consumption; body weight; weight gain; lung, kidney, and spleen mean weights; histopathology of liver, kidney, or lungs; percent pregnancy; no. of corpora lutea; no. of implants; total live or dead fetuses; no. of dead fetuses per litter; no. of resorptions per litter; percent litters with resorptions; and skeletal, visceral, or external parameters in fetuses. Significant differences (ANOVA, Duncan's multiple range test) relative to controls were observed in liver weights of the high dose group and in mean number of live fetuses per litter in both treatment groups.
[Battelle Pacific Northwest Laboratories; Teratologic Assessment of Ethylbenzene and 2-Ethoxyethanol with Cover Letter Dated 061887, (1981), EPA Document No. 86870000402, Fiche No. OTS0513150]
UNREVIEWED

Ethylbenzene (CAS# 100-41-4) was evaluated for developmental toxicity in 89, 77, and 77 female Wistar rats exposed to 0, 100, and 1000 ppm of the test material respectively by inhalation for 7 hours per day, 5 days per week for 3 weeks. They were then mated and exposed daily through the 19th day of gestation. The rats were killed and examined at the 21st day of gestation. No significant differences were observed in food consumption and body weights during progestational and gestational exposure periods. At 1000 ppm relative and absolute liver, spleen, and kidney weights were significantly greater than controls and or the 100 ppm group. No treatment-related histological changes were observed. Body weights, placenta weights, and sex ratios were all within normal limits. There were no significant increases in major malformations or minor anomalies. Litters were examined for the presence of external, visceral, and skeletal defects as well as the incidence of growth retardation and intrauterine mortality. A statistically significant increased incidence of fetal supernumary ribs was observed at the 1000 ppm exposure. It was concluded that ethylbenzene caused maternal and developmental toxicity (significant increase in extra ribs) at 1000 ppm.
[SHELL OIL CO; Teratogenic assessment of ethylbenzene and 2-ethoxyethanol; EPA 88-920002072, 1/01/81, Fiche No. OTS0539167]
UNREVIEWED

Ethylbenzene (CAS# 100-41-4) was evaluated for developmental toxicity in 24, 23, and 22 New Zealand white rabbits artificially inseminated and exposed for 7 hours daily to 0, 100, and 1000 ppm of the test material respectively until the 24th day of gestation. Neither maternal toxicity nor embryotoxicity was observed in rabbits exposed to ethylbenzene at 100 or 1000 ppm. Rabbits had increased maternal liver weights at 1000 ppm and reduced mean number of live fetuses at 100 and 1000 ppm. No significant differences were observed in food consumption and weight gain. No treatment-related organ weight or histopathological changes were observed. Fetal size (weight and length), placenta weights, and sex ratios were all within normal limits. The sex ratios of the groups were not affected by treatment. No statistically

significant incidences of major malformations, minor anomalies, or common variants were observed. It was concluded that the test material did not induce significant maternal toxicity, embryomortality, growth retardation, or teratogenicity at 1000 ppm.
[SHELL OIL CO; Teratogenic assessment of ethylbenzene and 2-ethoxyethanol; EPA 88-920002072, 1/01/81, Fiche No. OTS0539167] **UNREVIEWED**

The frequency of chromosomal aberrations was evaluated in vitro by exposing rats liver (RL1) cells to 25, 50 or 100 ug of ethyl benzene/ml. No increases in the frequency of chromatid gaps, chromatid breaks or total chromosome aberrations was observed at any dose level. Ethyl benzene did not induce chromosome damage in this assay.
[Shell Oil; In Vitro Genotoxicity Studies with Ethyl Benzene Hydroperoxide (EBHP) and Ethyl Benzene, (1981), EPA Doc. No. 86-870001656, Fiche No. OTS0515732] **UNREVIEWED**

The mutagenicity of ethyl benzene was evaluated in E. coli tester strains WP2 and WP2uvrA and in Salmonella tester strains TA98, TA100, TA1535, TA1537, and TA1538 (Ames test), both in the presence and absence of added metabolic activation by Aroclor-induced rat liver S9 fraction. Based on the results of preliminary bacterial toxicity determinations, ethyl benzene, in DMSO, was tested for mutagenicity at concentrations of 0.2, 2.0, 20.0, 200.0, and 2000.0 ug/plate using the direct plate incorporation method. Ethyl benzene did not cause a positive response in any of the tester strains with or without metabolic activation.
[Shell Oil; In Vitro Genotoxicity Studies with Ethyl Benzene Hydroperoxide (EBHP) and Ethyl Benzene, (1981), EPA Doc. No. 86-870001656, Fiche No. OTS0515732] **UNREVIEWED**

The ability of ethyl benzene to induce conversion of differentially inactive alleles to wild-type alleles in Saccharomyces cervisiae was examined in the mitotic gene conversion assay. The cultures were dosed with solutions of 20 ul (in the absence of added metabolic action provided by Aroclor-induced rat liver S9 fraction) or 25 ul (with S9) of 1, 10, 50, 100 or 500 mg ethyl benzene/ml. Ethyl benzene did not produce an increase mitotic gene conversion, either with or without added metabolic activation, and was not considered to be mutagenic in the assay.
[Shell Oil; In Vitro Genotoxicity Studies with Ethyl Benzene Hydroperoxide (EBHP) and Ethyl Benzene, (1981), EPA Doc. No. 86-870001656, Fiche No. OTS0515732] **UNREVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

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... RATS, RABBITS, GUINEA PIGS, AND MONKEYS /WERE EXPOSED/ TO CONCN OF ...

400-2200 PPM, 7 TO 8 HR/DAY, 5 DAYS A WK FOR AS LONG AS 6 MONTHS. THE GUINEA PIGS, RABBITS, AND MONKEYS WERE NOT AFFECTED ... SLIGHT INCREASE IN AVG WT OF KIDNEYS AND LIVERS WERE OBSERVED IN RATS EXPOSED TO 400 PPM FOR 186 DAYS.
[Patty, F. (ed.). Industrial Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New York: Interscience Publishers, 1963. 1232]**PEER REVIEWED**

... RATS /WERE INJECTED/ SUBCUTANEOUSLY WITH 1 ML ... PER KG OF BODY WT DAILY FOR 2 WEEKS AND ... NO DECREASE IN THE TOTAL FEMORAL MARROW NUCLEATED CELL COUNT /WAS OBSERVED/. THESE ANIMALS DEVELOPED A LEUCOCYTOSIS INSTEAD OF SEVERE LEUCOPENIAS FOUND IN BENZENE-DOSED ANIMALS WHICH SERVED AS POSITIVE CONTROLS.
[Patty, F. (ed.). Industrial Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New York: Interscience Publishers, 1963. 1232]**PEER REVIEWED**

EXPOSURE TO 2000 PPM FOR UP TO 375 MIN CAUSED IN SOME OF /GUINEA PIGS/ ... MOTOR ATAXIA AND APPARENT UNCONSCIOUSNESS; WITH 10,000 PPM THIS STAGE WAS REACHED IN 18 MIN. IT WAS PRECEDED BY VERTIGO, UNSTEADINESS AND ATAXIA.
[Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965. 92]**PEER REVIEWED**

LIVER & KIDNEY WT INCREASED IN RATS GIVEN SUBCHRONIC ORAL DOSES OF 408-680 MG/KG/DAY FOR 182 DAYS. /FROM TABLE/
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1345]**PEER REVIEWED**

INHALATION @ 3050 PPM (15 MG/L) PRODUCED LOSS OF RIGHTING RESPONSE IN MICE & DEATH IN 2 HR FROM 9150 PPM (45 MG/L). IN GUINEA PIGS 1000 PPM (4.92 MG/L)/3 MIN PRODUCED SLIGHT NASAL IRRITATION, @ 8 MIN EYE IRRITATION; 2000 PPM (9.84 MG/L)/1 MIN PRODUCED MODERATE EYE & NASAL IRRITATION, UNCONSCIOUSNESS @ 345 MIN. /FROM TABLE/
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1344]**PEER REVIEWED**

SUBACUTE EXPOSURE OF MALE RATS TO 2000 PPM PRODUCED INCREASES OF DOPAMINE & NORADRENALINE LEVELS & TURNOVER IN VARIOUS PARTS OF HYPOTHALAMUS & MEDIAN EMINENCE 16-18 HR FOLLOWING LAST EXPOSURE.
[ANDERSON K ET AL, TOXICOL APPL PHARMACOL 60 (3): 535 (1981)]**PEER REVIEWED**

Rats inhaling 600, 1200, or 2400 mg ethylbenzene/cu m for 24 hr/day from days 7-15 of pregnancy showed mild toxicity. The highest dose retarded skeletal development and weight gain in the fetuses and increased the incidence of extra ribs. Sacral displacement with abnormal development was observed in 2 instances. Thus, ethylbenzene, has some embryotoxic and teratogenic activity.

[Tatrai E et al; Egeszsegtudomany 26 (3): 297-303 (1982)]**PEER REVIEWED**

Ethylbenzene was investigated ... as a sensory irritant in mice. The concn necessary to depress the respiratory rate by 50% (RD 50) due to sensory irritation of the upper respiratory tract was 4060 ppm. ... A model for the sensory irritating action ... was proposed on the basis of ... physical interaction with a receptor protein.
[Nielsen GD, Alarie Y; Toxical Appl Pharmacol 65 (3): 459-77 (1982)]**PEER REVIEWED**

Drop application to rabbit eyes caused slight irritation and no corneal injury demonstrable by fluorescein staining. Standard testing on rabbit eyes gave an injury grade of 2 on a scale of 10.
[Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986. 413]**PEER REVIEWED**

Rats were exposed for 3 days by inhalation to 2000 ppm of a xylene mixture, or ... ethylbenzene. All solvents increased hepatic cytochrome p450 concn and NADPH-cytochrome C reductase activity. The ability of ethylbenzene to modify the metabolism of other potentially toxic substances in liver, kidney, and lung microsomes suggested the possibility of synergistic toxic responses.
[Toftgard R, Nilsen OG; Toxicol 23 (2-3): 197-212 (1982)]**PEER REVIEWED**

Concn of < 0.25 mg/l can cause tainting of fish flesh.
[Cleland, J.G., G.L. Kingsbury. Multimedia Environmental Goals for Environmental Assessment. Volume 1. EPA-600/7-77-136a. Research Triangle Park, NC: EPA, Nov. 1977.,p. E-148]**PEER REVIEWED**

Neither maternal toxicity nor embryotoxicity was observed in gravid rabbits exposed to ethylbenzene /by inhalation/ at 100 or 1000 ppm.
[NIOSH; Teratologic Assessment of Ethylbenzene and 2-Ethoxyethanol p.iii (1981) NIOSH Contract No. 210-79-0037]**PEER REVIEWED**

Neither maternal toxicity nor embyrotoxicity was observed /in pregnant rats/ exposed to ethylbenzene /by inhalation/ at 100 ppm ... but /1000 ppm/ induced some indications of toxicity. ... A significant increase in the incidence of extra ribs was detected in rat fetuses exposed in utero to the high level.
[NIOSH; Teratologic Assessment of Ethylbenzene and 2-Ethoxyethanol p.iii (1981) NIOSH Contract No. 210-79-0037]**PEER REVIEWED**

Mice, B6C3F1 Fischer-344 rats, and /rabbits /New Zealand/ (five/sex/group) were exposed by inhalation to ethylbenzene vapors for 6 hr/day, 5 days/week for 4 weeks (20 exposures). Rats and mice received 0, 99, 382, or 782 ppm ethylbenzene while rabbits received 0, 382, 782, or 1610 ppm. No changes were evident in mortality patterns, clinical chemistries, urinalyses, or treatment-related gross/microscopic (including ophthalmologic) lesions. Rats exhibited sporadic lacrimation and salivation, as well as significantly increased liver weights at 382 and 782 ppm, and small increases in leukocyte counts at 782 ppm. Males at this exposure level also showed marginal elevations in platelet counts. In mice, females showed statistically increased absolute and relative liver weights at 382 and 782 ppm while males had statistically increased relative liver-to-brain weight ratios only at 782 ppm. Female rabbits at the high exposure level of 1610 ppm gained weight more slowly than controls (not statistically significant); males

showed a similar transient downward trend after 1 week, but showed no differences from controls at study's end. A no observed adverse effect level (NOAEL) of 382 ppm appears appropriate for rats and mice with a lowest observed adverse effect level (LOAEL) of 782 ppm. A NOAEL of 782 ppm and LOAEL of 1610 ppm are appropriate for rabbits.
[Cragg ST et al; Fundam Appl Toxicol 13 (3): 399-408 (1989)]**PEER REVIEWED**

Repeated application of undiluted ethyl benzene to the ear and shaved abdominal area of rabbits (10-20 applications over a period of 2-4 wk) resulted in erthyema, edema, and superficial necrosis. ... Two drops of ethyl benzene into the conjunctival sac produced only a slight irritation of the conjunctival membranes but no corneal injury.
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Volumes I,II, III. Cincinnati, OH: ACGIH, 1991. 581]**PEER REVIEWED**

Inhalation of 2600 mg/cu m (600 ppm) ethyl benzene 7 hr/day, 5 days/wk for 186 days caused degeneration of the germinal epithelium in the testes of rabbits and monkeys but not of rats. Pregnant rats exposed at 100 or 1000 ppm 6 hr/day for 3 wk prior to mating and on days 1-19 of gestation had pups with a significant increase ($p < 0.05$) in extra rib formation; at the higher dose, maternal toxicity was indicated by increased liver, kidney, and spleen weights.
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Volumes I,II, III. Cincinnati, OH: ACGIH, 1991. 582]**PEER REVIEWED**

... CONCLUSIONS: Under the conditions of these 2 yr inhalation studies, there was clear evidence of carcinogenic activity of ethylbenzene in male F344/N rats based on incr incidences of renal tubule neoplasms. The incidences of testicular adenoma were also incr. There was some evidence of carcinogenic activity of ethylbenzene in female F344/N rats based on incr incidences of renal tubule adenomas. There was some evidence of carcinogenic activity of ethylbenzene in male B6C3F1 mice based on incr incidences of alveolar/bronchiolar neoplasms. There was some evidence of carcinogenic activity of ethylbenzene in female B6C3F1 mice based on incr incidences of hepatocellular neoplasms.
[Toxicology & Carcinogenesis Studies of Ethylbenzene in F344/N Rats and B6C3F1 Mice p.5 Technical Report Series No. 466 (1999) NIH Publication No. 99-3956 U.S. Department of Health and Human Services, National Toxicology Program, National Institute of Environmental Health Sciences, Research Triangle Park, NC 27709]**PEER REVIEWED**

ETHYLBENZENE

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National Toxicology Program Studies:

... 2 Yr Study in Rats: Groups of 50 male and 50 female F344/N rats were exposed to 0, 75, 250 or 750 ppm ethylbenzene 6 hr day, 5 days/wk for 104 wk. ... 2 Yr Study in Mice: Groups of 50 male and 50 female B6C3F1 mice were exposed to 0, 75, 250 or 750 ppm ethylbenzene by inhalation, 6 hr/day, 5 days/wk for 103 wk. ... CONCLUSIONS: Under the conditions of these 2 yr inhalation studies, there was clear evidence of carcinogenic activity of ethylbenzene in male F344/N rats based on incr incidences of renal tubule neoplasms. The incidences of testicular adenoma were also incr. There was some evidence of carcinogenic activity of ethylbenzene in female F344/N rats based on incr incidences of renal tubule adenomas. There was some evidence of carcinogenic activity of ethylbenzene in male B6C3F1 mice based on incr incidences of alveolar/bronchiolar neoplasms. There was some evidence of carcinogenic activity of ethylbenzene in female B6C3F1 mice based on incr incidences of hepatocellular neoplasms. [Toxicology & Carcinogenesis Studies of Ethylbenzene in F344/N Rats and B6C3F1 Mice p.5 Technical Report Series No. 466 (1999) NIH Publication No. 99-3956 U.S. Department of Health and Human Services, National Toxicology Program, National Institute of Environmental Health Sciences, Research Triangle Park, NC 27709]**QC REVIEWED**

ETHYLBENZENE

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Non-Human Toxicity Values:

LD50 Rat oral 5.46 g/kg.
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 643]**PEER REVIEWED**

LD50 Rat oral 3500 mg/kg
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1522]**PEER REVIEWED**

LD50 Mouse ip 2272 mg/kg
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1522]**PEER REVIEWED**

LD50 Rabbit skin 17,800 mg/kg
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1522]**PEER REVIEWED**

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Ecotoxicity Values:

LC50 Lepomis macrochirus 32 mg/l/96 hr /Conditions of bioassay not specified/
[Pickering QH, Henderson C; J Water Pollut Control Fed 38: 1419 (1966)]**PEER REVIEWED**

LC50 Carassius auratus 94.44 mg/l/96 hr /Conditions of bioassay not specified/
[Pickering QH, Henderson C; J Water Pollut Control Fed 38: 1419 (1966)]**PEER REVIEWED**

LC50 Lebistes reticulatus 97.10 mg/l/96 hr /Conditions of bioassay not specified/
[Pickering QH, Henderson C; J Water Pollut Control Fed 38: 1419 (1966)]**PEER REVIEWED**

LC50 Mysidopsis bahia (shrimp) 87.6 mg/l 96 hr in a static unmeasured bioassay
[USEPA; In-depth Studies on Health Environmental Impacts of Selected Water Pollutants (1978) EPA No 68-01-4646]**PEER REVIEWED**

LC50 Cyprinodon variegatus (sheepshead minnow) 275 mg/l 96 hr in a static unmeasured bioassay
[USEPA; In-depth Studies on Health Environmental Impacts of Selected Water Pollutants (1978) EPA No 68-01-4646]**PEER REVIEWED**

LC50 Pimephales promelas (fathead minnow) 42.3 (hardwater) to 48.5 (softwater) mg/l 96 hr /Conditions of bioassay not specified/
[Pickering OH, Henderson C; J Water Pollut Control Fed 38: 1419 (1966)]**PEER REVIEWED**

LC50 Poecilla reticulata (guppy) 97.1 mg/l/96 hr /Conditions of bioassay not specified/
[Pickering OH, Henderson C; J Water Pollut Control Fed 38: 1419 (1966)]**PEER REVIEWED**

Toxicity threshold (cell multiplication inhibition test): Microcystis aeruginosa (algae) 33 mg/l; Scenedesmus quadricauda (green algae) > 160 mg/l
[Verschueren, K. Handbook of Environmental Data on Organic Chemicals. 3rd ed. New York, NY: Van Nostrand Reinhold Co., 1996. 946]**PEER REVIEWED**

Toxicity threshold (cell multiplication inhibition test): Entosiphon sulcatum (protozoa) 140 mg/l; Uronema parduczi Chatton-Lwoff (protozoa) > 110 mg/l.
[Verschueren, K. Handbook of Environmental Data on Organic Chemicals. 3rd ed. New York, NY: Van Nostrand Reinhold Co., 1996. 946]**PEER REVIEWED**

Toxicity threshold (cell multiplication inhibition test): Pseudomonas putida (bacteria) 12 mg/l.
[Verschueren, K. Handbook of Environmental Data on Organic Chemicals.

3rd ed. New York, NY: Van Nostrand Reinhold Co., 1996. 946]**PEER REVIEWED**

LC50 Palaemonetes pugio (grass shrimp, adult) 14,400 ug/l/24 hr in a static unmeasured bioassay [USEPA; Ambient Water Quality Criteria Doc: Ethylbenzene p.3-7 (1980) EPA 440/5-80-048]**PEER REVIEWED**

LC50 Palaemonetes pugio (grass shrimp, larva) 10,200 ug/l/24 hr in a static unmeasured bioassay [USEPA; Ambient Water Quality Criteria Doc: Ethylbenzene p.3-7 (1980) EPA 440/5-80-048]**PEER REVIEWED**

LC50 Pimephales promelas (fathead minnow) 12.1 mg/l/96 hr (confidence limit 11.5 - 12.7 mg/l), flow-through bioassay with measured concentrations, 26.1 deg C, dissolved oxygen 7.0 mg/l, hardness 45.6 mg/l calcium carbonate, alkalinity 43.0 mg/l calcium carbonate, and pH 7.39. [Geiger D.L., Poirier S.H., Brooke L.T., Call D.J., eds. Acute Toxicities of Organic Chemicals to Fathead Minnows (Pimephales Promelas). Vol. III. Superior,Wisconsin: University of Wisconsin-Superior, 1986. 189]**PEER REVIEWED**

ETHYLBENZENE

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TSCA Test Submissions:

In a single generation reproduction study, 380 female and 60 male Wistar rats were exposed to ethylbenzene at average daily concentrations of 97 or 959 ppm 7 hours per day, 5 days per week for 3 weeks. They were then mated and exposed daily on gestation days (GD) 1-19 at concentrations of 96 (low) or 985 (high) ppm. Animals were sacrificed and examined on GD 21. No significant differences were observed between treatment groups and controls in food consumption, gestational body weights (of pregnant rats), organ weights (of male rats), histopathology of liver, kidney or lungs, percent pregnancy, no. of corpora lutea, no. of implants, total live or dead fetuses, no. of live or dead fetuses per litter, no. of resorptions per litter and percent litters with resorptions. A significant difference (ANOVA, Duncan's multiple range test) was observed in pregestational body weights in both treatment groups. Maternal toxicity was indicated in the high dose groups (dosed at the high level during both periods or dosed with air during pregestational and with the high level during gestation) by significant differences (ANOVA, Duncan's multiple range test) in liver, spleen and kidney weights. Statistically significant differences were seen in mean crown-rump length (in the group which was dosed at the high level during both periods), supernumerary ribs (in the 2 high dose groups and the group which was dosed with air pregestationally and with the low level during gestation) and rudimentary rib incidence (in the group dosed with air during pregestation and with the high level during gestation).
[Battelle Pacific Northwest Laboratories; Teratologic Assessment of Ethylbenzene and 2-Ethoxyethanol with Cover Letter Dated 061887, (1981), EPA Document No. 86870000402, Fiche No. OTS0513150]
UNREVIEWED

In a single generation reproduction study 96 New Zealand White rabbits were artifically inseminated and exposed to ethylbenzene at average daily concentrations of 99 or 962 ppm 7 hours per day, through gestation day (GD) 24. Animals were sacrificed and examined on GD 30. Mortality was observed in 2 does, 1 from each dose group. No significant differences were observed between treatment groups and controls in the following: food consumption; body weight; weight gain; lung, kidney, and spleen mean weights; histopathology of liver, kidney, or lungs; percent pregnancy; no. of corpora lutea; no. of implants; total live or dead fetuses; no. of dead fetuses per litter; no. of resorptions per litter; percent litters with resorptions; and skeletal, visceral, or external parameters in fetuses. Significant differences (ANOVA, Duncan's multiple range test) relative to controls were observed in liver weights of the high dose group and in mean number of live fetuses per litter in both treatment groups.
[Battelle Pacific Northwest Laboratories; Teratologic Assessment of Ethylbenzene and 2-Ethoxyethanol with Cover Letter Dated 061887, (1981), EPA Document No. 86870000402, Fiche No. OTS0513150]
UNREVIEWED

Ethylbenzene (CAS# 100-41-4) was evaluated for developmental toxicity in 89, 77, and 77 female Wistar rats exposed to 0, 100, and 1000 ppm of the test material respectively by inhalation for 7 hours per day, 5 days per week for 3 weeks. They were then mated and exposed daily through the 19th day of gestation. The rats were killed and examined at the 21st day of gestation. No significant differences were observed in food consumption and body weights during progestational and gestational exposure periods.

At 1000 ppm relative and absolute liver, spleen, and kidney weights were significantly greater than controls and or the 100 ppm group. No treatment-related histological changes were observed. Body weights, placenta weights, and sex ratios were all within normal limits. There were no significant increases in major malformations or minor anomalies. Litters were examined for the presence of external, visceral, and skeletal defects as well as the incidence of growth retardation and intrauterine mortality. A statistically significant increased incidence of fetal supernumary ribs was observed at the 1000 ppm exposure. It was concluded that ethylbenzene caused maternal and developmental toxicity (significant increase in extra ribs) at 1000 ppm.
[SHELL OIL CO; Teratogenic assessment of ethylbenzene and 2-ethoxyethanol; EPA 88-920002072, 1/01/81, Fiche No. OTS0539167] **UNREVIEWED**

Ethylbenzene (CAS# 100-41-4) was evaluated for developmental toxicity in 24, 23, and 22 New Zealand white rabbits artificially inseminated and exposed for 7 hours daily to 0, 100, and 1000 ppm of the test material respectively until the 24th day of gestation. Neither maternal toxicity nor embryotoxicity was observed in rabbits exposed to ethylbenzene at 100 or 1000 ppm. Rabbits had increased maternal liver weights at 1000 ppm and reduced mean number of live fetuses at 100 and 1000 ppm. No significant differences were observed in food consumption and weight gain. No treatment-related organ weight or histopathological changes were observed. Fetal size (weight and length), placenta weights, and sex ratios were all within normal limits. The sex ratios of the groups were not affected by treatment. No statistically significant incidences of major malformations, minor anomalies, or common variants were observed. It was concluded that the test material did not induce significant maternal toxicity, embryomortality, growth retardation, or teratogenicity at 1000 ppm.
[SHELL OIL CO; Teratogenic assessment of ethylbenzene and 2-ethoxyethanol; EPA 88-920002072, 1/01/81, Fiche No. OTS0539167] **UNREVIEWED**

The frequency of chromosomal aberrations was evaluated in vitro by exposing rats liver (RL1) cells to 25, 50 or 100 ug of ethyl benzene/ml. No increases in the frequency of chromatid gaps, chromatid breaks or total chromosome aberrations was observed at any dose level. Ethyl benzene did not induce chromosome damage in this assay.
[Shell Oil; In Vitro Genotoxicity Studies with Ethyl Benzene Hydroperoxide (EBHP) and Ethyl Benzene, (1981), EPA Doc. No. 86-870001656, Fiche No. OTS0515732] **UNREVIEWED**

The mutagenicity of ethyl benzene was evaluated in E. coli tester strains WP2 and WP2uvrA and in Salmonella tester strains TA98, TA100, TA1535, TA1537, and TA1538 (Ames test), both in the presence and absence of added metabolic activation by Aroclor-induced rat liver S9 fraction. Based on the results of preliminary bacterial toxicity determinations, ethyl benzene, in DMSO, was tested for mutagenicity at concentrations of 0.2, 2.0, 20.0, 200.0, and 2000.0 ug/plate using the direct plate incorporation method. Ethyl benzene did not cause a positive response in any of the tester strains with or without metabolic activation.
[Shell Oil; In Vitro Genotoxicity Studies with Ethyl Benzene Hydroperoxide (EBHP) and Ethyl Benzene, (1981), EPA Doc. No. 86-870001656, Fiche No. OTS0515732] **UNREVIEWED**

The ability of ethyl benzene to induce conversion of differentially inactive alleles to wild-type alleles in

Saccharomyces cervisiae was examined in the mitotic gene conversion assay. The cultures were dosed with solutions of 20 ul (in the absence of added metabolic action provided by Aroclor-induced rat liver S9 fraction) or 25 ul (with S9) of 1, 10, 50, 100 or 500 mg ethyl benzene/ml. Ethyl benzene did not produce an increase mitotic gene conversion, either with or without added metabolic activation, and was not considered to be mutagenic in the assay.
[Shell Oil; In Vitro Genotoxicity Studies with Ethyl Benzene Hydroperoxide (EBHP) and Ethyl Benzene, (1981), EPA Doc. No. 86-870001656, Fiche No. OTS0515732] **UNREVIEWED**

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Metabolism/Pharmacokinetics:

Metabolism/Metabolites:

ETHYL BENZENE IN MAN IS METABOLIZED 64% TO MANDELIC AND 25% TO PHENYLGLYOXYLIC ACID AND EXCRETED INTO URINE.
[Thienes, C., and T.J. Haley. Clinical Toxicology. 5th ed. Philadelphia: Lea and Febiger, 1972. 126]**PEER REVIEWED**

THE OXIDATION OF ETHYLBENZENE TO METHYLPHENYLCARBINOL IN ANIMALS ... WAS CONFIRMED ... WITH ADDITIONAL FINDING THAT BOTH ISOMERS OF METHYL PHENYL CARBINOL (THE + AND - FORMS) IN EQUAL AMT ARE RESULT OF ITS BIOLOGICAL HYDROXYLATION.
[Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965. 91]**PEER REVIEWED**

In the rabbit, it is metabolized to a number of oxidation products and subsequently excreted. The major urinary metabolite is hippuric acid. The oxidation products are benzoic acid, phenylacetic acid, and mandelic acid, excreted as the glycine conjugate, and also methylphenylcarbinol, 1-phenylethanol, excreted as the glucuronide.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1343]**PEER REVIEWED**

FROM A DOSE OF 100 MG/KG ADMIN ORALLY TO RATS ... THE URINARY METABOLITES, P-ETHYLPHENOL, ABOUT 0.3%, & SMALLER QUANTITIES OF 1- & 2-PHENYLETHANOL /WERE IDENTIFIED/.
[Clayton, G. D. and F. E. Clayton (eds.). Patty's Industrial Hygiene and Toxicology: Volume 2A, 2B, 2C: Toxicology. 3rd ed. New York: John Wiley Sons, 1981-1982. 3304]**PEER REVIEWED**

URINARY SULFATE RATIO DECREASES ARE NORMALLY A ROUGH EST OF DOSE-RELATED ALKYLBENZENE HYDROXYLATION DUE MAINLY TO SIDE CHAIN OXIDATION. ... THIS ... DOES NOT HOLD WITH DOSE-ACTION RELATIONSHIP FOR ETHYLBENZENE. ... AT HIGH DOSES, RING HYDROXYLATION INCREASES, ALTERING SULFATE RATIO.
[Clayton, G. D. and F. E. Clayton (eds.). Patty's Industrial Hygiene and Toxicology: Volume 2A, 2B, 2C: Toxicology. 3rd ed. New York: John Wiley Sons, 1981-1982. 3304]**PEER REVIEWED**

PRODUCTS OF RING HYDROXYLATION ... DETECTED FOR 1ST TIME IN RABBIT URINE. ... IDENTIFICATION OF M- & P-HYDROXYACETOPHENONE & ... ACETOPHENONE REVEALS THAT FURTHER OXIDATION IN SIDE-CHAIN OF ACETOPHENONE TO PHENACYL ALCOHOL (& THEN TO BENZOIC ACID) IS NOT ONLY PATHWAY. ... HOWEVER,

RING-HYDROXYLATED PRODUCTS ARE ONLY MINOR ONES.
[The Chemical Society. Foreign Compound Metabolism in Mammals. Volume 4: A Review of the Literature Published during 1974 and 1975. London: The Chemical Society, 1977. 247]**PEER REVIEWED**

SINCE ... (1+) & (-1)METHYLPHENYL CARBINOL YIELDED (-1)MANDELIC ACID /IN RATS/, AS DID ACETOPHENONE & OMEGA-HYDROXYACETOPHENONE, THE STEREOSELECTIVE STEP MUST OCCUR DURING OXIDATION &/OR REDUCTION OF LATTER ... EITHER PATHWAY IS POSSIBLE, FOR ... PHENYLGLYOXAL & ... PHENYLETHYLENE GLYCOL ... YIELDED (-)MANDELIC ACID STEREOSELECTIVELY.
[The Chemical Society. Foreign Compound Metabolism in Mammals. Volume 5: A Review of the Literature Published during 1976 and 1977. London: The Chemical Society, 1979. 505]**PEER REVIEWED**

BENZOYLFORMIC ACID WAS BY-PRODUCT IN ALL ... EXPT /IN WHICH RATS WERE FED POSSIBLE INTERMEDIATES/. HOWEVER, WHEN THIS CMPD WAS FED, NO MANDELIC ACID WAS FORMED, & NEITHER WAS (-1)MANDELIC ACID CONVERTED INTO BENZOYLFORMIC ACID.
[The Chemical Society. Foreign Compound Metabolism in Mammals. Volume 5: A Review of the Literature Published during 1976 and 1977. London: The Chemical Society, 1979. 505]**PEER REVIEWED**

FEMALE ASSISTANTS USING MIXTURE OF XYLENES & ETHYLBENZENE AS SOLVENT IN HISTOLOGY LAB WERE EXAM. AVG AIR CONCN OF (M + P)-XYLENE & ETHYLBENZENE WAS BETWEEN 56-68 & 34-41 PPM. APPROX 1.1 TO 1.4% OF RETAINED ETHYLBENZENE WAS METABOLIZED TO 2-ETHYL-PHENOL.
[ANGERER J ET AL; INT ARCH OCCUP ENVIRON HEALTH 43 (2): 145 (1979)]**PEER REVIEWED**

IN 3 LAB TECHNICIANS OCCUPATIONALLY EXPOSED TO ETHYLBENZENE, THE URINARY METABOLITES WERE AMYGDALIC ACID, PHENYLGLYOXYLIC ACID & 2-ETHYLPHENOL; WITHIN 24 HR MORE THAN 90% OF METABOLITES HAD BEEN EXCRETED.
[HAGEMANN J ET AL; KREBSGEFAEHRDUNG ARBEITSPLATZ/ARBEITSMED KOLLOQ, BER JAHRESTAG DTSCH GES ARBEITSMED, 19TH: 421 (1979)]**PEER REVIEWED**

After ip administration of /4.45 g/ ethylbenzene /to rabbits/ ... o-, p-, and m-hydroxyacetophenone were identified in urine. The above hydroxyacetophenones represented 0.11, 0.13, and 0.03% of the dose ... respectively.
[Kiese M, Lenk W; Xenobiotica 4: 337-43 (1974)]**PEER REVIEWED**

WHEN ABSORBED THROUGH SKIN, MANDELIC ACID WAS EXCRETED AT 4.6%, WHEREAS AFTER LUNG ABSORPTION MAJORITY OF ETHYLBENZENE WAS CONVERTED TO MANDELIC ACID & CONJUGATED WITH GLYCINE.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1343]**PEER REVIEWED**

After 2 volunteers were exposed to 65 ppm ethylbenzene for 3 hr, the metabolites of ethylbenzene in

their urine, mandelic acid, hippuric acid (HA), and phenylglyoxylic (PhGA) were analyzed. The metabolites were excreted in the urine in the order mandelic acid > hippuric acid > phenylglyoxylic. The highest value of excretion was observed 6-10 hr after the beginning of exposure. Mandelic acid/phenylglyoxylic and hippuric/phenylglyoxylic mol ratios of total excretion in urine were 3.5 and 2.6 respectively.
[Yamasaki Y; Okayama Igakkai Zasshi 96 (5/6): 531-5 (1984)]**PEER REVIEWED**

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[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Volumes I,II, III. Cincinnati, OH: ACGIH, 1991. 583]**PEER REVIEWED**

Absorption, Distribution & Excretion:

ABSORPTION IS CHIEFLY BY INHALATION. A SMALL PROPORTION ... THAT GETS INTO THE BLOOD STREAM IS EXHALED UNCHANGED, BUT MOST OF IT /70%/ IS FOUND IN THE URINE AS METABOLITES BECAUSE OF OXIDATION OF THE SIDE CHAIN.
[Patty, F. (ed.). Industrial Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New York: Interscience Publishers, 1963. 1232]**PEER REVIEWED**

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THREE LAB TECHNICIANS EXPOSED TO 42 PPM & 1 TO 34 PPM HAD AVG STEADY STATE BLOOD LEVELS OF 0.72 + OR - 0.11 MG/L. 30 MIN AFTER EXPOSURE CONCN HAD DROPPED TO APPROX 0.5% OF ORIGINAL VALUES.
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After exposure to 112-156 mg/l (aq) the skin absorption rate in humans (n= 14) was 0.11 to 0.21 mg/sq m/hr.
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[USEPA; Ambient Water Quality Criteria Doc: Ethylbenzene p.C-6 (1980) EPA 440/5-80-048]**PEER REVIEWED**

After exposure of rats to atmospheres of 50, 300, or 600 ppm ethylbenzene 6 hr/day, 5 days/wk, for

maximum of 16 wk, the concn of ethylbenzene in perirenal fat and the urinary excretion of 1-phenylethanol, omega-hydroxyacetophenone, mandelic acid, phenylglyoxylic acid, hippuric acid, and phenaceturic acid were measured at the 2nd, 5th, and 9th weeks. Excretion of metabolites into urine increased in a dose-related manner, but less than linearly. The level of exposure, but not the duration of exposure, markedly affected the pattern of the metabolites in the urine. The concn of ethylbenzene in perirenal fat was low at 50 ppm, high at 300 ppm and higher still at 600 ppm, but not in proportion to the increased dose.
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Percutaneous absorption of benzene, toluene, ethylbenzene, and aniline was investigated in male HRS/J hairless mice. Stainless steel skin depots containing 100 to 150 mg of solid sorbent were fixed to the backs of anesthetized mice and charged with about 5 ul of (14)C tagged test solution. Expired air samples were obtained until 4 hours after exposure, when mice were killed and samples for radioactivity were obtained from the skin depot, the skin under the depot, a wiping of the skin under the depot, the carcass, feces, urine, and cage washings. Physical constants were determined for each test compound, including octanol/water partition coefficient, solubility, vapor pressure, melting and boiling points, and absorption and evaporation rates. Solvent recovery exceeded 90% in all mice with highest recovery in the skin depot. Average administered doses were 3.94 mg benzene, of which 0.99% was absorbed; 3.89 mg toluene (2.31% absorbed), 4.10 mg ethylbenzene (3.61% absorbed), and 4.68 mg aniline (4.76% absorbed). Excretion rate in expired air was fastest during the first 15 minutes of exposure except in mice treated with toluene or ethylbenzene, which demonstrated maximal excretion rate during the second 15 minutes after exposure. A two compartment model was suggested by the initial rapid and subsequent gradual decay of expired breath excretion. Vapor pressure and boiling point were significantly correlated with the applied radioactive dose absorbed. Absorption rates were found to be 56, 49, 37, and 2.3 ug per square centimeter per minute for benzene, toluene, ethylbenzene, and aniline, respectively.
[Susten AS et al; J Appl Toxicol 10 (3): 217-25 (1990)]**PEER REVIEWED**

Mechanism of Action:

The effect of styrene, toluene, ethylbenzene, alpha-methylstyrene, and butylbenzene on oxidative phosphorylation was studied using rat liver mitochondrial preparations. Rat liver mitochondria were prepared from male white Wistar rats and assessed for respiration rate, oxygen uptake, glutamate oxidation, succinate oxidation, ATPase activity, and proton permeability in the presence and absence of the alkyl benzene derivatives. Inclusion of the alkyl benzene derivatives in the incubation medium produced an initial acceleration of oxygen consumption followed by an inhibition of glutamate oxidation, and the stimulatory effect paralleled the aliphatic chain length. Glutamate oxidation was also inhibited by styrene, ethylbenzene, and alpha-methylstyrene but not by butylbenzene or toluene in 2,4-dinitrophenol uncoupled mitochondria. Styrene and the aliphatic benzene derivative stimulated succinate oxidation in rat liver mitochondria without effect on 2,4-dinitrophenol stimulated succinate oxidation. Similar stimulatory effects on ATPase activity were observed with maximal stimulation occurring at the same relative concentrations producing maximal succinate oxidation. ATPase stimulation required magnesium, was oligomycin sensitive, and showed an inverse relation to the hydrophobicity of the compounds tested. The inclusion of styrene in the incubation medium markedly increased the rate of passive entry of protons into rat liver mitochondria in a manner comparable to 2,4-dinitrophenol. It was concluded that styrene and other monosubstituted benzene derivatives act as mitochondrial uncoupling agents.
[Mickiewicz W, Rzeczycki W; Biochem Pharmacol 37 (23): 4439-44

(1988)]**PEER REVIEWED**

Effect of monocyclic aromatic hydrocarbons, their metabolites, and their structure on brain dopamine was studied. Adult male New Zealand rabbits were exposed to 750 ppm toluene, styrene, ethylbenzene, vinyltoluene, 7-methylstyrene, xylenes, and fresh air. Six groups of eight rabbits received 4 mM/kg ip for 3 days of hippuric acid, mandelic acid, methylhippuric acid, phenylglyoxylic acid, or 7-methylmandelic acid. Animals were killed 12 hours after inhalation exposure or 24 hours after the last dose of acid. The hypothalamus, striatum, hippocampus, tuberoinfundibular area, and part of the brain cortex were treated with 0.2 molar perchloric acid, homogenized, desorbed on alumina, and centrifuged. Supernatant was filtered and used to measure homovanillic acid. Styrene induced a marked dopamine depletion and a significant increase in homovanillic acid concentration. Ethylbenzene and vinyltoluene produced a smaller, but statistically significant effect. Toluene, xylenes, and 7-methylstyrene were ineffective. Phenylglyoxylic acid caused a decrease in dopamine levels and a consistent rise in homovanillic acid in striatal and tuberoinfundibular regions. Mandelic acid elicited the same effect, but to a lesser degree. 7-Methylmandelic, methylhippuric, and hippuric acids evoked no response. Neither solvents nor their metabolites affected norepinephrine contents of brain areas in which this neurotransmitter reaches high concentrations. It was concluded that the results indicate that the changes in brain dopamine depend on metabolic interferences of some metabolites of aromatic solvents with dopamine catabolism. Only metabolites whose side chain may be transformed into a alpha-keto acid caused dopamine depletion.
[Romanelli A et al; J Appl Toxicol 6 (6): 431-5 (1986)]**PEER REVIEWED**

The effect of organic solvents on the CNS was discussed. The similarity of effects of different solvents is believed to be due to the formation of tetrahydroisoquinolines by nonenzymatic condensation of dopamine with metabolites of organic solvents having a reactive carbonyl group. The suspected metabolites are phenylglyoxylic- acid that is formed by metabolism of ethylbenzene, styrene, vinyltoluene; trichloroacetaldehyde, which derives from trichloroethylene, tetrachloroethylene; and trichloroethane; glyoxylic acid that is synthesized from ethyleneglycol and ethyleneglycolmonomethyl ether; formaldehyde that is metabolized from methanol; and acetaldehyde that is transformed from ethanol. The tuberoinfundibular dopaminergic system may represent a target for metabolites dissolved in the blood stream. The suggested mechanism implies a selective vulnerability of pituitary functions. The impairment of tuberoinfundibular activity may explain most of the behavioral changes observed with styrene and perhaps with other similar solvents. It appears that the majority of pathways that are affected in the hypothalamic control of gonadotropins in primates are adrenergic and dopaminergic. Occupational exposure to neurotoxins may cause repeated reversible CNS effects which are difficult to distinguish from the chronic effects. In workers exposed to styrene a relationship between recent exposure and measurable effects on CNS has been observed and prolonged exposure has failed to induce tolerance. It was concluded that although no excessive risk for Alzheimer disease and presenile dementia has been found, there is no indication that exposure to solvents does not cause irreversible or slowly reversible cognitive or neuropsychological impairment.
[Mutti A, Franchini I; Br J Ind Med 44 (11): 721-3 (1987)]**PEER REVIEWED**

Efforts were made to clarify the molecular basis of styrene toxicity on the dopaminergic systems and to evaluate whether the same mechanism was common to other solvents. Groups of male New Zealand rabbits were exposed to 750 ppm toluene, xylene, styrene, ethylbenzene, vinyltoluene, 7-methyl-styrene, or fresh air (control group). A significant depletion in both striatal and tubero infundibular dopamine was

caused styrene, ethylbenzene, and vinyltoluene. Methylation of the aromatic ring of styrene did not change its activity, whereas methylation of the side chain drastically reduced its effect on dopamine. Treatments carried out with the main metabolites of aromatic solvents indicated that acidic metabolites of some solvents cause striatal and tubero infundibular dopamine depletion. Present data suggested a chemical reaction between dopamine and some acidic metabolites. The active metabolites have an alpha-keto acid as the side chain or as a part of their molecule. These keto acids condense nonenzymatically with dopamine in both experimental models and in occupational exposed workers as evidenced by the direct measurements of dopamine in the brain. According to the authors, such a mechanism may account for neurobehavioral effects resulting from solvent exposure such as mood changes, or impaired attention spans and decreasing psychomotor performance factors.
[Mutti A et al; Toxicol 49 (1, part 1): 77-82 (1988)]**PEER REVIEWED**

Interactions:

IN LAB ASSISTANTS USING XYLENES & ETHYLBENZENE, 2,4-DIMETHYLPHENOL, METAB OF M-XYLENE COULD NOT BE DETECTED. COMPETITIVE REACTION BETWEEN XYLENES & ETHYLBENZENE PREVENTED M-XYLENE FROM OXIDATION. ...
[ANGERER J ET AL; INT ARCH OCCUP ENVIRON HEALTH 43 (2): 145 (1979)]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Metabolism/Metabolites:

ETHYL BENZENE IN MAN IS METABOLIZED 64% TO MANDELIC AND 25% TO PHENYLGLYOXYLIC ACID AND EXCRETED INTO URINE.
[Thienes, C., and T.J. Haley. Clinical Toxicology. 5th ed. Philadelphia: Lea and Febiger, 1972. 126]**PEER REVIEWED**

THE OXIDATION OF ETHYLBENZENE TO METHYLPHENYLCARBINOL IN ANIMALS ... WAS CONFIRMED ... WITH ADDITIONAL FINDING THAT BOTH ISOMERS OF METHYL PHENYL CARBINOL (THE + AND - FORMS) IN EQUAL AMT ARE RESULT OF ITS BIOLOGICAL HYDROXYLATION.
[Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965. 91]**PEER REVIEWED**

In the rabbit, it is metabolized to a number of oxidation products and subsequently excreted. The major urinary metabolite is hippuric acid. The oxidation products are benzoic acid, phenylacetic acid, and mandelic acid, excreted as the glycine conjugate, and also methylphenylcarbinol, 1-phenylethanol, excreted as the glucuronide.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1343]**PEER REVIEWED**

FROM A DOSE OF 100 MG/KG ADMIN ORALLY TO RATS ... THE URINARY METABOLITES, P-ETHYLPHENOL, ABOUT 0.3%, & SMALLER QUANTITIES OF 1- & 2-PHENYLETHANOL /WERE IDENTIFIED/.
[Clayton, G. D. and F. E. Clayton (eds.). Patty's Industrial Hygiene and Toxicology: Volume 2A, 2B, 2C: Toxicology. 3rd ed. New York: John Wiley Sons, 1981-1982. 3304]**PEER REVIEWED**

URINARY SULFATE RATIO DECREASES ARE NORMALLY A ROUGH EST OF DOSE-RELATED ALKYLBENZENE HYDROXYLATION DUE MAINLY TO SIDE CHAIN OXIDATION. ... THIS ... DOES NOT HOLD WITH DOSE-ACTION RELATIONSHIP FOR ETHYLBENZENE. ... AT HIGH DOSES, RING HYDROXYLATION INCREASES, ALTERING SULFATE RATIO.
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PRODUCTS OF RING HYDROXYLATION ... DETECTED FOR 1ST TIME IN RABBIT URINE. ... IDENTIFICATION OF M- & P-HYDROXYACETOPHENONE & ... ACETOPHENONE REVEALS THAT FURTHER OXIDATION IN SIDE-CHAIN OF ACETOPHENONE TO PHENACYL ALCOHOL (& THEN TO BENZOIC ACID) IS NOT ONLY PATHWAY. ... HOWEVER, RING-HYDROXYLATED PRODUCTS ARE ONLY MINOR ONES.
[The Chemical Society. Foreign Compound Metabolism in Mammals. Volume

4: A Review of the Literature Published during 1974 and 1975. London: The Chemical Society, 1977. 247]**PEER REVIEWED**

SINCE ... (1+) & (-1)METHYLPHENYL CARBINOL YIELDED (-1)MANDELIC ACID /IN RATS/, AS DID ACETOPHENONE & OMEGA-HYDROXYACETOPHENONE, THE STEREOSELECTIVE STEP MUST OCCUR DURING OXIDATION &/OR REDUCTION OF LATTER ... EITHER PATHWAY IS POSSIBLE, FOR ... PHENYLGLYOXAL & ... PHENYLETHYLENE GLYCOL ... YIELDED (-)MANDELIC ACID STEREOSELECTIVELY.
[The Chemical Society. Foreign Compound Metabolism in Mammals. Volume 5: A Review of the Literature Published during 1976 and 1977. London: The Chemical Society, 1979. 505]**PEER REVIEWED**

BENZOYLFORMIC ACID WAS BY-PRODUCT IN ALL ... EXPT /IN WHICH RATS WERE FED POSSIBLE INTERMEDIATES/. HOWEVER, WHEN THIS CMPD WAS FED, NO MANDELIC ACID WAS FORMED, & NEITHER WAS (-1)MANDELIC ACID CONVERTED INTO BENZOYLFORMIC ACID.
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FEMALE ASSISTANTS USING MIXTURE OF XYLENES & ETHYLBENZENE AS SOLVENT IN HISTOLOGY LAB WERE EXAM. AVG AIR CONCN OF (M + P)-XYLENE & ETHYLBENZENE WAS BETWEEN 56-68 & 34-41 PPM. APPROX 1.1 TO 1.4% OF RETAINED ETHYLBENZENE WAS METABOLIZED TO 2-ETHYL-PHENOL.
[ANGERER J ET AL; INT ARCH OCCUP ENVIRON HEALTH 43 (2): 145 (1979)]**PEER REVIEWED**

IN 3 LAB TECHNICIANS OCCUPATIONALLY EXPOSED TO ETHYLBENZENE, THE URINARY METABOLITES WERE AMYGDALIC ACID, PHENYLGLYOXYLIC ACID & 2-ETHYLPHENOL; WITHIN 24 HR MORE THAN 90% OF METABOLITES HAD BEEN EXCRETED.
[HAGEMANN J ET AL; KREBSGEFAEHRDUNG ARBEITSPLATZ/ARBEITSMED KOLLOQ, BER JAHRESTAG DTSCH GES ARBEITSMED, 19TH: 421 (1979)]**PEER REVIEWED**

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[Kiese M, Lenk W; Xenobiotica 4: 337-43 (1974)]**PEER REVIEWED**

WHEN ABSORBED THROUGH SKIN, MANDELIC ACID WAS EXCRETED AT 4.6%, WHEREAS AFTER LUNG ABSORPTION MAJORITY OF ETHYLBENZENE WAS CONVERTED TO MANDELIC ACID & CONJUGATED WITH GLYCINE.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1343]**PEER REVIEWED**

After 2 volunteers were exposed to 65 ppm ethylbenzene for 3 hr, the metabolites of ethylbenzene in their urine, mandelic acid, hippuric acid (HA), and phenylglyoxylic (PhGA) were analyzed. The metabolites were excreted in the urine in the order mandelic acid > hippuric acid > phenylglyoxylic. The

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Percutaneous absorption of benzene, toluene, ethylbenzene, and aniline was investigated in male HRS/J hairless mice. Stainless steel skin depots containing 100 to 150 mg of solid sorbent were fixed to the backs of anesthetized mice and charged with about 5 ul of (14)C tagged test solution. Expired air samples were obtained until 4 hours after exposure, when mice were killed and samples for radioactivity were obtained from the skin depot, the skin under the depot, a wiping of the skin under the depot, the carcass, feces, urine, and cage washings. Physical constants were determined for each test compound, including octanol/water partition coefficient, solubility, vapor pressure, melting and boiling points, and absorption and evaporation rates. Solvent recovery exceeded 90% in all mice with highest recovery in the skin depot. Average administered doses were 3.94 mg benzene, of which 0.99% was absorbed; 3.89 mg toluene (2.31% absorbed), 4.10 mg ethylbenzene (3.61% absorbed), and 4.68 mg aniline (4.76% absorbed). Excretion rate in expired air was fastest during the first 15 minutes of exposure except in mice treated with toluene or ethylbenzene, which demonstrated maximal excretion rate during the second 15 minutes after exposure. A two compartment model was suggested by the initial rapid and subsequent gradual decay of expired breath excretion. Vapor pressure and boiling point were significantly correlated with the applied radioactive dose absorbed. Absorption rates were found to be 56, 49, 37, and 2.3 ug per square centimeter per minute for benzene, toluene, ethylbenzene, and aniline, respectively.
[Susten AS et al; J Appl Toxicol 10 (3): 217-25 (1990)]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Mechanism of Action:

The effect of styrene, toluene, ethylbenzene, alpha-methylstyrene, and butylbenzene on oxidative phosphorylation was studied using rat liver mitochondrial preparations. Rat liver mitochondria were prepared from male white Wistar rats and assessed for respiration rate, oxygen uptake, glutamate oxidation, succinate oxidation, ATPase activity, and proton permeability in the presence and absence of the alkyl benzene derivatives. Inclusion of the alkyl benzene derivatives in the incubation medium produced an initial acceleration of oxygen consumption followed by an inhibition of glutamate oxidation, and the stimulatory effect paralleled the aliphatic chain length. Glutamate oxidation was also inhibited by styrene, ethylbenzene, and alpha-methylstyrene but not by butylbenzene or toluene in 2,4-dinitrophenol uncoupled mitochondria. Styrene and the aliphatic benzene derivative stimulated succinate oxidation in rat liver mitochondria without effect on 2,4-dinitrophenol stimulated succinate oxidation. Similar stimulatory effects on ATPase activity were observed with maximal stimulation occurring at the same relative concentrations producing maximal succinate oxidation. ATPase stimulation required magnesium, was oligomycin sensitive, and showed an inverse relation to the hydrophobicity of the compounds tested. The inclusion of styrene in the incubation medium markedly increased the rate of passive entry of protons into rat liver mitochondria in a manner comparable to 2,4-dinitrophenol. It was concluded that styrene and other monosubstituted benzene derivatives act as mitochondrial uncoupling agents.
[Mickiewicz W, Rzeczycki W; Biochem Pharmacol 37 (23): 4439-44 (1988)]**PEER REVIEWED**

Effect of monocyclic aromatic hydrocarbons, their metabolites, and their structure on brain dopamine was studied. Adult male New Zealand rabbits were exposed to 750 ppm toluene, styrene, ethylbenzene, vinyltoluene, 7-methylstyrene, xylenes, and fresh air. Six groups of eight rabbits received 4 mM/kg ip for 3 days of hippuric acid, mandelic acid, methylhippuric acid, phenylglyoxylic acid, or 7-methylmandelic acid. Animals were killed 12 hours after inhalation exposure or 24 hours after the last dose of acid. The hypothalamus, striatum, hippocampus, tuberoinfundibular area, and part of the brain cortex were treated with 0.2 molar perchloric acid, homogenized, desorbed on alumina, and centrifuged. Supernatant was filtered and used to measure homovanillic acid. Styrene induced a marked dopamine depletion and a significant increase in homovanillic acid concentration. Ethylbenzene and vinyltoluene produced a smaller, but statistically significant effect. Toluene, xylenes, and 7-methylstyrene were ineffective. Phenylglyoxylic acid caused a decrease in dopamine levels and a consistent rise in homovanillic acid in striatal and tuberoinfundibular regions. Mandelic acid elicited the same effect, but to a lesser degree. 7-Methylmandelic, methylhippuric, and hippuric acids evoked no response. Neither solvents nor their metabolites affected norepinephrine contents of brain areas in which this neurotransmitter reaches high concentrations. It was concluded that the results indicate that the changes in brain dopamine depend on metabolic interferences of some metabolites of aromatic solvents with dopamine catabolism. Only metabolites whose side chain may be transformed into a alpha-keto acid caused dopamine depletion.
[Romanelli A et al; J Appl Toxicol 6 (6): 431-5 (1986)]**PEER REVIEWED**

The effect of organic solvents on the CNS was discussed. The similarity of effects of different solvents is believed to be due to the formation of tetrahydroisoquinolines by nonenzymatic condensation of

dopamine with metabolites of organic solvents having a reactive carbonyl group. The suspected metabolites are phenylglyoxylic- acid that is formed by metabolism of ethylbenzene, styrene, vinyltoluene; trichloroacetaldehyde, which derives from trichloroethylene, tetrachloroethylene; and trichloroethane; glyoxylic acid that is synthesized from ethyleneglycol and ethyleneglycolmonomethyl ether; formaldehyde that is metabolized from methanol; and acetaldehyde that is transformed from ethanol. The tuberoinfundibular dopaminergic system may represent a target for metabolites dissolved in the blood stream. The suggested mechanism implies a selective vulnerability of pituitary functions. The impairment of tuberoinfundibular activity may explain most of the behavioral changes observed with styrene and perhaps with other similar solvents. It appears that the majority of pathways that are affected in the hypothalamic control of gonadotropins in primates are adrenergic and dopaminergic. Occupational exposure to neurotoxins may cause repeated reversible CNS effects which are difficult to distinguish from the chronic effects. In workers exposed to styrene a relationship between recent exposure and measurable effects on CNS has been observed and prolonged exposure has failed to induce tolerance. It was concluded that although no excessive risk for Alzheimer disease and presenile dementia has been found, there is no indication that exposure to solvents does not cause irreversible or slowly reversible cognitive or neuropsychological impairment.
[Mutti A, Franchini I; Br J Ind Med 44 (11): 721-3 (1987)]**PEER REVIEWED**

Efforts were made to clarify the molecular basis of styrene toxicity on the dopaminergic systems and to evaluate whether the same mechanism was common to other solvents. Groups of male New Zealand rabbits were exposed to 750 ppm toluene, xylene, styrene, ethylbenzene, vinyltoluene, 7-methyl-styrene, or fresh air (control group). A significant depletion in both striatal and tubero infundibular dopamine was caused styrene, ethylbenzene, and vinyltoluene. Methylation of the aromatic ring of styrene did not change its activity, whereas methylation of the side chain drastically reduced its effect on dopamine. Treatments carried out with the main metabolites of aromatic solvents indicated that acidic metabolites of some solvents cause striatal and tubero infundibular dopamine depletion. Present data suggested a chemical reaction between dopamine and some acidic metabolites. The active metabolites have an alpha-keto acid as the side chain or as a part of their molecule. These keto acids condense nonenzymatically with dopamine in both experimental models and in occupational exposed workers as evidenced by the direct measurements of dopamine in the brain. According to the authors, such a mechanism may account for neurobehavioral effects resulting from solvent exposure such as mood changes, or impaired attention spans and decreasing psychomotor performance factors.
[Mutti A et al; Toxicol 49 (1, part 1): 77-82 (1988)]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Interactions:

IN LAB ASSISTANTS USING XYLENES & ETHYLBENZENE, 2,4-DIMETHYLPHENOL, METAB OF M-XYLENE COULD NOT BE DETECTED. COMPETITIVE REACTION BETWEEN XYLENES & ETHYLBENZENE PREVENTED M-XYLENE FROM OXIDATION. ...
[ANGERER J ET AL; INT ARCH OCCUP ENVIRON HEALTH 43 (2): 145 (1979)]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Pharmacology:

Interactions:

IN LAB ASSISTANTS USING XYLENES & ETHYLBENZENE, 2,4-DIMETHYLPHENOL, METAB OF M-XYLENE COULD NOT BE DETECTED. COMPETITIVE REACTION BETWEEN XYLENES & ETHYLBENZENE PREVENTED M-XYLENE FROM OXIDATION. ...
[ANGERER J ET AL; INT ARCH OCCUP ENVIRON HEALTH 43 (2): 145 (1979)]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Environmental Fate & Exposure:

Environmental Fate/Exposure Summary:

Ethylbenzene's production and use as an intermediate for the production of styrene, its presence in automotive and aviation fuels, and its presence in crude oil may result in its release to the environment through various waste streams. If released to air, a vapor pressure of 9.6 mm Hg at 25 deg C indicates ethylbenzene will exist solely as a vapor in the ambient atmosphere. Vapor-phase ethylbenzene will be degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals; the half-life for this reaction in air is estimated to be 55 hr. If released to soil, ethylbenzene is expected to have moderate mobility based upon an estimated Koc of 520. Volatilization from moist soil surfaces is expected to be an important fate process based upon a Henry's Law constant of 7.88X10-3 atm-cu m/mole. Ethylbenzene may volatilize from dry soil surfaces based upon its vapor pressure. Biodegradation in soil takes place via nitrate-reducing processes. If released into water, ethylbenzene may adsorb to suspended solids and sediment in water based upon the estimated Koc. Biodegradation in a gasoline contaminated aquifer ranged from 10-16 days under aerobic conditions. Ethylbenzene was degraded in 8 days in groundwater and 10 days in seawater as a component of gas oil. Volatilization from water surfaces is expected to be an important fate process based upon this compound's Henry's Law constant. Estimated volatilization half-lives for a model river and model lake are 1.1 and 99 hrs, respectively. Measured BCFs of 0.67 to 15 suggest the potential for bioconcentration in aquatic organisms is low. Hydrolysis is not expected to occur due to the lack of hydrolyzable functional groups. Occupational exposure to ethylbenzene may occur through inhalation at municipal waste composting facilities and via inhalation and dermal contact with this compound at workplaces where ethylbenzene is produced or used. The general population may be exposed to ethylbenzene via inhalation of ambient air, drinking and eating contaminated foods and water, and by handling gasoline. Ethylbenzene is likely to be detected in groundwater. (SRC)
PEER REVIEWED

Probable Routes of Human Exposure:

NIOSH (NOES Survey 1981-1983) has statistically estimated that 80,726 workers (21,785 of these are female) are potentially exposed to ethylbenzene in the US(1). Occupational exposure to ethylbenzene may occur via inhalation at municipal waste composting facilities where the air concn was found to be 78,000-178,000 ug/cu m(2),and through inhalation and dermal contact with this compound at worplaces where ethylbenzene is produced or used(SRC). The general population may be exposed to ethylbenzene via inhalation of ambient air, ingestion of foods and fish, and drinking contaminated water, and dermal contact with this compound and other products such as gasoline which contains ethylbenzene(SRC).
[(1) NIOSH; National Occupational Exposure Survey (NOES) (1983) (2) Eitzer BD; Environ Sci Technol 29: 896-902 (1995)]**PEER REVIEWED**

Body Burden:

Ethylbenzene was detected, not quantified, in 8 of 8 samples of mother's milk from 4 US urban areas(1).

16.5% of 387 expired air samples taken from 54 normal, healthy, urban volunteers were positive for ethylbenzene concn with an avg of 1.8 ng/l expired air(2). Whole blood samples from 250 subjects ranged in ethylbenzene concns from not detected to 59 ppb, with an avg of 1.0 ppb(3).
[(1) Pellizzari ED et al; Bull Environ Contam Toxicol 28: 322-8 (1982) (2) Krotoszynski BK et al; J Anal Toxicol 3: 225-34 (1979) (3) Antoine SR et al; Bull Environ Contam Toxicol 36: 364-71 (1986)]**PEER REVIEWED**

Average Daily Intake:

AIR INTAKE: (assume air concn of 0.2-2.7 ppb)(2-6); 17-235 ug; WATER INTAKE: (assume water concn of 0-4 ppb(1)) 0-8 ug; FOOD INTAKE: insufficient data(SRC).
[(1) Konasewich D et al; Status Report on Organic and Heavy Metal Contaminants in the Lake Erie, Michigan, Huron and Superior Basins. Great Lakes Quality Review Board (1978) (2) Arnts RR, Meeks SA; Biogenic Hydrocarbon Contribution to the Ambient Air of Selected Areas p. 31 USEPA-600/3-80-023 (1980) (3) Atshuller AP et al; Environ Sci Technol 5: 1009-16 (1981) (4) Lonneman WA et al; Environ Sci Technol 2: 1017-20 (1968) (5) Singh HB et al; Atmos Environ 15: 601-12 (1981) (6) Singh HB et al; Atmospheric Measurements of Selected Toxic Organic Chemicals USEPA-600/3-80-072 (1980)]**PEER REVIEWED**

Natural Pollution Sources:

Ethylbenzene is a product of biomass combustion(1), and a component of crude oil(2).
[(1) Graedel TE; Atmospheric Chemical Compounds. New York NY Academic Press (1986) (2) Nunes P, Benville PE JR; Bull Environ Contam Toxicol 21: 71-24 (1979)]**PEER REVIEWED**

Artificial Pollution Sources:

Ethylbenzene is present at 0.02 wt% in coke-oven tars.
[Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984.,p. V22 572 (1983)]**PEER REVIEWED**

Ethylbenzene's production and use as an intermediate for the manufacture of styrene and use as a resin solvent(1), intermediate for the production of diethylbenzene and acetophenone(2), and its use as a component of automotive and aviation fuels(3) may result in its release to the environment through various waste streams.
[(1) Budavari S, ed; The Merck Index. 12th ed. Whitehouse Station, NJ: Merck and Co., Inc. p. 643 (1996) (2) Coty RR et al; Ullmann's Encycl Indust Chem. 5th ed. Deerfield Beach, FL: VCH Pub A 10: 35-43 (1985) (3) Clayton GB, Clayton FE; Patty's Industrial Hygiene and Toxicology. 2B: Toxicology. 4th ed. NY, NY: John Wiley & Sons Inc 2B: 1342 (1994)]**PEER REVIEWED**

Environmental Fate:

TERRESTRIAL FATE: Based on a classification scheme(1), an estimated Koc value of 520(SRC), determined from a structure estimation method(2), indicates that ethylbenzene is expected to have moderate mobility in soil(SRC). Volatilization of ethylbenzene from moist soil surfaces is expected to be an important fate process(SRC) given a Henry's Law constant of 7.88X10-3 atm-cu m/mole(3). The potential for volatilization of ethylbenzene from dry soil surfaces may exist(SRC) based upon a vapor pressure of 9.6 mm Hg(4). Ethylbenzene was completely degraded in microcosms inoculated with the sediment material from a refinery pond or activated sludge from the refinery treatment facility under nitrate-reducing conditions(5). At Sleeping Bear Dunes National Lakeshore in Michigan, ethylbenzene was degraded at slow rates via anaerobic degradation under ambient subsurface conditions using ferric iron, sulfate and/or carbon dioxide as the terminal electron acceptors(6).
[(1) Swann RL et al; Res Rev 85: 17-28 (1983) (2) Meylan WM et al; Environ Sci Technol 26: 1560-67 (1992) (3) Sanemasa I et al; Bull Chem Soc Japan 55: 1054-62 (1982) (4) Daubert TE et al; Physical and Thermodynamic Properties of Pure Chemicals. NY, NY: Hemisphere Pub Corp (1989) (5) Ball HA et al; pp. 458-63 in In-Situ Bioreclamation. Hinchee RE, Olfenbuttel RF, eds. Boston, MA: Butterworth-Heinemann (1991) (6) Borden RC et al; Anaerobic biodegradation of BTEX in aquifer material. USEPA/600/S-97/003 pp. 9 (1997)]**PEER REVIEWED**

AQUATIC FATE: Based on a classification scheme(1), an estimated Koc value of 520(SRC), determined from an estimation method(2), indicates that ethylbenzene may adsorb to suspended solids and sediment(SRC). Volatilization from water surfaces is expected(3) based upon a Henry's Law constant of 7.88X10-3 atm-cu m/mole(4). Using this Henry's Law constant and an estimation method(3), volatilization half-lives for a model river and model lake are 1.1 and 99 hr, respectively(SRC). According to a classification scheme(5), an experimental log BCF of 1.19(7), which corresponds to a BCF of 15, suggests the potential for bioconcentration in aquatic organisms is low. In a shallow coastal plain aquifer contaminated with gasoline and diesel fuel in rural Sampson County in North Carolina, ethylbenzene was degraded in aerobic conditions within 10-16 days and in conditions of low initial oxygen, it was rapidly degraded in 21 days until the available oxygen was depleted(8). As a component of gas oil, ethylbenzene is completely degraded in groundwater in 8 days(9) and seawater in 10 days(10). In a mesocosm experiment using simulated Narragansett Bay conditions, complete biodegradation occurred in approximately 2 days after a 2 week lag in spring and a 2 day lag in summer(11).
[(1) Swann RL et al; Res Rev 85: 17-28 (1983) (2) Meylan WM et al; Environ Sci Technol 26: 1560-67 (1992) (3) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington, DC: Amer Chem Soc pp. 4-9, 15-1 to 15-29 (1990) (4) Sanemasa I et al; Bull Chem Soc Japan 55: 1054-62 (1982) (5) France C et al; Chemosphere 29: 1501-14 (1994) (6) Hansch C et al; Exploring QSAR. Hydrophobic, Electronic, and Steric Constants. ACS Prof Ref Book. Heller SR, consult. ed., Washington, DC: Amer Chem Soc p. 43 (1995) (7) Park JH, Lee HJ; Chemosphere 26: 1905-16 (1993) (8) Borden RC et al; Water Resour Res 33: 1105-15 (1996) (9) Kappeler T, Wuhrmann K; Water Res 12: 327-33 (1978) (10) Van der Linden AC; Dev Biodegrad Hydrocarbons 1: 165-200 (1978) (11) Wakeham SG et al; Environ Sci Technol 17: 611-7 (1983)]**PEER REVIEWED**

ATMOSPHERIC FATE: According to a model of gas/particle partitioning of semivolatile organic compounds in the atmosphere(1), ethylbenzene, which has a vapor pressure of 9.6 mm Hg at 25 deg C(2), is expected to exist solely as a vapor. Vapor-phase ethylbenzene is degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals(SRC); the half-life for this reaction in air is 55 hr(SRC), calculated from its rate constant of 7.1X10-12 cu cm/molecule-sec at 25 deg C(3).
[(1) Bidleman TF; Environ Sci Technol 22: 361-367 (1988) (2) Daubert TE et al; Physical & Thermodynamic Properties of Pure Chemicals NY, NY: Hemisphere Pub Corp (1989) (3) Atkinson R; J Phys Chem Ref Data Monograph No. 2 p. 48 (1994)]**PEER REVIEWED**

Environmental Biodegradation:

After a period of inocula adaptation, ethylbenzene is biodegraded fairly rapidly by sewage or activated sludge inoculua(1-3,9). As a component of gas oil, it is completely degraded in groundwater in 8 days(4) and seawater in 10 days(5). In a mesocosm experiment using simulated Narragansett Bay conditions, complete biodegradation occurred in approximately 2 days after a 2 week lag in spring and a 2 day lag in summer(6). Part of the attenuation in concn from a leaky gasoline storage tank in the chalk aquifer in England has been attributed to biodegradation(7). No degradation was observed in an anaerobic reactor even after 110 days acclimation(8) or at low concentrations in a batch reactor in 11 weeks under denitrifying conditions(10). Percent removal in an anaerobic, continuous-flow, laboratory bioflim column was 7% after a 2 day detention time(11); 99% removal was observed in a similar aerobic column following a 20 min detention time(11).
[(1) Slave T et al; Rev Chim 25: 666-70 (1974) (2) Tabak HH et al; J Water Pollut Control Fed 53: 1503-18 (1981) (3) Malaney GW, McKinney RE; Water Sewage Works 113: 302-9 (1966) (4) Kappeler T, Wuhrmann K; Water Res 12: 327-33 (1978) (5) Van der Linden AC; Dev Biodegrad Hydrocarbons 1: 165-200 (1978) (6) Wakeham SG et al; Environ Sci Technol 17: 611-7 (1983) (7) Tester DJ, Harker RJ; Water Pollut Control 80: 614-31 (1981) (8) Chou WL et al; Biotechnol Bioeng Symp 8: 391-414 (1979) (9) USEPA; Treatability Manual p 1.9.8-1 to 1.9.8-5 USEPA 600/2-82-001a (1981) (10) Bouwer EJ, McCarty PL; Appl Environ Microbiol 45: 1295-99 (1983) (11) Bouwer EJ, McCarthy PL; Ground Water 22: 433-40 (1984)]**PEER REVIEWED**

AEROBIC: A study was conducted using underground storage tanks containing gasoline and diesel fuel that contaminated a shallow coastal plain aquifer in rural Sampson County in North Carolina. Ethylbenzene was degraded in aerobic conditions within 10-16 days and in conditions of low initial oxygen, it was rapidly degraded in 21 days until the available oxygen was depleted(1). A combined culture experiment of Mycobacterium vaccae and Rhodococcus sp. strain R-22 showed M. vaccae alone and M. vaccae and R-22 together can oxidize ethylbenzene to 4-ethylphenol which is then degraded to 50 ppm within 72 hr(2).
[(1) Borden RC et al; Water Resour Res 33: 1105-15 (1996) (2) Fairlee JR et al; J Microbiol 43: 841-6 (1997)]**PEER REVIEWED**

ANAEROBIC: Anaerobic ethylbenzene transformation in Seal Beach Naval Weapons Station sediments in Southern California appeared to be strictly associated with nitrate-reducing processes(1). Ethylbenzene was completely degraded in microcosms inoculated with the sediment material from a refinery pond or

activated sludge from the refinery treatment facility under nitrate-reducing conditions(2). At Sleeping Bear Dunes National Lakeshore in Michigan, ethylbenzene was degraded at slow rates via anaerobic degradation under ambient subsurface conditions using ferric iron, sulfate and/or carbon dioxide as the terminal electron acceptors(3).
[(1) Ball HA, Reinhard M; Environ Toxicol Chem 15: 114-22 (1996) (2) Ball HA et al; pp. 458-63 in In-Situ Bioreclamation. Hinchee RE, Olfenbuttel RF, eds. Boston, MA: Butterworth-Heinemann (1991) (3) Borden RC et al; Anaerobic biodegradation of BTEX in aquifer material. USEPA/600/S-97/003 pp. 9 (1997)]**PEER REVIEWED**

Environmental Abiotic Degradation:

The rate constant for the vapor-phase reaction of ethylbenzene with photochemically-produced hydroxyl radicals is 7.1X10-12 cu cm/molecule-sec at 298 K(1) which corresponds to an atmospheric half-life of about 55 hr at an atmospheric concn of 5X10+5 hydroxyl radicals per cu cm. Ethylbenzene is not expected to undergo hydrolysis in the environment due to the lack of hydrolyzable functional groups(2). Ethylbenzene photolysis occurs via photooxidation hydrogen abstraction from the alkyl group by photooxydatively formed hydroxyl radical which results in the formation of acetophenone, and eventually benzaldehyde with 2-butanedial, 4-oxo-2-hexenal, and 2-ethyl-2-butenedial being suggested as further end products(3).
[(1) Atkinson R; J Phys Chem Ref Data Monograph No. 2 p. 48 (1994) (2) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington, DC: Amer Chem Soc pp. 7-4, 7-5 (1990) (3) Forstner HJL et al; Environ Sci Technol 31: 1345-58 (1997)]**PEER REVIEWED**

Environmental Bioconcentration:

Experimental data on the bioconcentration of ethylbenzene include a log BCF of 1.9 in goldfish(2) and a log BCF of 0.67 for clams exposed to the water-soluble fraction of crude oil(1). Experimentally, a log BCF of 1.19 has also been reported(4) which corresponds to a BCF of 15. According to a classification scheme(3), these BCFs suggest the potential for bioconcentration in aquatic organisms is low.
[(1) Nunes P, Benville PE Jr; Bull Environ Contam Toxicol 21: 719-24 (1979) (2) Ogata M et al; Bull Environ Contam Toxicol 33: 561-7 (1984) (3) Franke C et al; Chemosphere 29: 1501-14 (1994) (4) Park JH, Lee HJ; Chemosphere 26: 1905-16 (1993)]**PEER REVIEWED**

Soil Adsorption/Mobility:

Using a structure estimation method based on molecular connectivity indices(1), the Koc for ethylbenzene can be estimated to be 520(SRC). According to a classification scheme(2), this estimated Koc value suggests that ethylbenzene is expected to have low mobility in soil.
[(1) Meylan WM et al; Environ Sci Technol 26: 1560-67 (1992) (2) Swann RL et al; Res Rev 85: 17-28 (1983)]**PEER REVIEWED**

Volatilization from Water/Soil:

The Henry's Law constant for ethylbenzene is 7.88X10-3 atm-cu m/mole(1). This Henry's Law constant indicates that ethylbenzene will volatilize from water surfaces(2). Based on this Henry's Law constant, the volatilization half-life from a model river (1 m deep, flowing 1 m/sec, wind velocity of 3 m/sec)(2) is

estimated as 1.1 hr(SRC). The volatilization half-life from a model lake (1 m deep, flowing 0.05 m/sec, wind velocity of 0.5 m/sec)(2) is estimated as 99 hr(SRC). Ethylbenzene's Henry's Law constant(1) indicates that volatilization from moist soil surfaces may occur(SRC). The potential for volatilization of ethylbenzene from dry soil surfaces may exist(SRC) based upon a vapor pressure of 9.6 mm Hg(3).
[(1) Sanemasa I et al; Bull Chem Soc Jpn 55: 1054-62 (1982) (2) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington, DC: Amer Chem Soc pp. 15-1 to 15-29 (1990) (3) Daubert TE et al; Physical & Thermodynamic Properties of Pure Chemicals NY, NY: Hemisphere Pub Corp (1989)]**PEER REVIEWED**

Environmental Water Concentrations:

DRINKING WATER: In surveys of representative US municipal water supplies, ethylbenzene has been detected in most cases(1,2,4-8,10). Values for 3 New Orleans finished drinking waters ranged 1.6 to 2.3 ppb(6). Chicago Central Water Works on Lake Michigan measured 4 ppb(8). It has been found in the water supply for Evansville, IN on the Ohio River(7). 6 of 10 US cities were found to be positive(1,4). One US city had 1 of 4 samples pos with a 1 ppb avg, while another reported no positive samples(5). Tap water from bank infiltrated Rhine River water in the Netherlands measured 30 ppb in one study(3). Zurich, Switzerland tap water - detected not quantified(9). 1982 US groundwater supply survey, random samples of finished water supplies using groundwater as a source, 466 random samples, 0.6%, pos (0.5 ppb detection limit), 0.8 ppb median, 1.1 ppb max(10).
[(1) NAS; The Alkylbenzenes p III-13 Contract 68-01-4655 (1980) (2) Shackelford WM, Keith, LH; Frequency of Organic Compounds in Surface Waters USEPA 600/4-76-062 (1976) (3) Piet GJ, Morra CF; p 31-42 in Artificial Groundwater Recharge; Huisman L, Olsthorn TN, eds (1983) (4) Bedding ND et al; Sci Total Environ 25: 143-67 (1982) (5) Callahan MA et al; p 55-61 in 8th Natl Conf Munic Sludge Manage Proc (1979) (6) Keith, LH et al; p 329-73 in Identification and Analysis of Organic Pollutants in Water. Keith LH ed (1976) (7) Kleopfer RD, Fairless BJ; Environ Sci Technol 6: 1036-7 (1972) (8) Konasewich D et al; Status Report on Organic and Heavy Metal Contaminants in the Lakes Erie, Michigan, Huron and Superior Basins. Great Lakes Quality Review Board (1978) (9) Santodonato J et al; Investigation of selected potential environmental contaminants: styrene, ethylbenzene and related compounds 261 p USEPA 560/11-80-018 (1980) (10) Cotruvo JA; Sci Technol Environ 47: 7-26 (1985)]**PEER REVIEWED**

GROUNDWATER: A well in Ames, IA measured 15 ppb 50 yr after tar residues were buried at a nearby coal gas plant(5). Concns of 82-400 ppb were detected in two aquifers near the Hoe Creek underground coal gasification site in Wyoming, 15 mo after gasification was complete(2). In a US survey, 1970-76, it was detected but not quantified in well waters(1). In Jackson Township, NJ, drinking water wells measured 2000 ppb(4). Chalk aquifer in East Anglia, England - 210 m from petroleum storage - 0.15 ppb, 10 m distance - 1110 ppb, and 100-200 m - <250 ppb(3).
[(1) Shackelford WM, Keith, LH; Frequency of Organic Compounds Identified in Water USEPA 600/4-76-062 (1976) (2) Stuermer DH et al; Environ Sci Technol 16: 582-7 (1982) (3) Tester DH, Harker RJ; Water Pollut Control 80: 614-31 (1981) (4) Burmaster DE; Environ 24: 6-13,

33-6 (1982) (5) Santodonato J et al; Investigation of Selected Potential Environmental Contaminants: Styrene, Ethylbenzene and Related Compounds 261 p USEPA 560/11-80-018 (1980)]**PEER REVIEWED**

SURFACE WATER: Ethylbenzene has been detected but not quantified in a 1970-76 US survey(1,4). 14 heavily industrialized US river basins, 5 of 204 sites pos - 1-4 ppb; Chicago area and Illinois River Basin, 5 of 31 sites pos - 1-4 ppb(6). Two representative US cities, city A - 41% of 28 samples pos, 5.0 ppb avg, city B - 40% of 48 samples pos 3.2 ppb avg(2). Lower Tennessee River near Calvert City, KY reported 4.0 ppb(7). Lake Michigan, Chicago Sanitary and Ship Channel measured 1-2 ppb(3). River Glatt, Switzerland -detected, not quantified(5). USEPA STORET database, 1,101 data points, 10% pos, <5.0 ppb median(8).
[(1) Shackelford WM, Keith LH; Frequency of Organic Compounds Identified in Water USEPA 600/4-76-062 (1976) (2) Callahan MA et al; p 55-61 in 8th Natl Conf Munic Sludge Manage Proc (1979) (3) Konasewich D et al; Status Report on Organic and Heavy Metal Contaminants in the Lakes Erie, Michigan, Huron and Superior Basins. Great Lakes Quality Review Board (1978) (4) Bertsch W et al; J Chromatogr 112: 701-18 (1975) (5) Zuercher F, Giger W; Vom Wasser 47: 37-55 (1976) (6) Ewing BB et al; Monitoring to Detect Previously Unrecognized Pollutants in Surface Waters 75 p USEPA 560/6-77-015 (appendix USEPA 560/6-77-015a) (1977) (7) Goodley PG, Gordon M; Kentucky Acad Sci 37: 11-5 (1976) (8) Staples CA et al; Environ Toxicol Chem 4: 131-42 (1985)]**PEER REVIEWED**

SEAWATER: Ethylbenzene concns were found to be 30-50 ng/l in an estuary in Brazos, US; between <10-46.3 ng/l in UK; and 36.9 ng/l in Belgium(1). Ethylbenzene has been found in concns of 4.5-30 ng/l in Vineyard Sound; 0.4-4.5 ng/l in coastal and shelf sea water in the Gulf of Mexico; 5.5-22 ng/l in the coastal waters of Spain; 4.3-380 ng/l in Campeche Shelf; <10 ng/l in shelf and bay waters in UK; and 9.4-18.7 ng/l in Belgian Continental Shelf(1). Ethylbenzene mean concn of 21.94 ng/l was found in the South Northern sea up to 60 km offshore in the Scheldt Estuary(2). In the coastal waters off the western Gulf of Mexico at the mouth of the Brazos River, TX, ethylbenzene concns range between 0.004-0.5 ug/l(3). In the Gulf of Mexico in unpolluted areas ethylbenzene concn is 0.4 to 5 ppb(4,6), while an area of anthropogenic influence ranged from 5 to 15 ppb(6). Cape Cod, MA measured ethylbenzene at 22 ppb(5,7) with 11 ppb being avg(5). In the coastal waters of the Dutch Northern Sea, 108 samples ranged from not detected to 20 parts per trillion and averaged 4 parts per trillion(8).
[(1) Dewulf J, Vanlangenhove H; Water Res 31: 1825-38 (1997) (2) Dewulf JP et al; Environ Sci Technol 32: 903-11 (1998) (3) Neff JM, Sauer TC Jr; Environ Sci Res 52: 163-75 (1996)(4) Sauer TC Jr et al; Mar Chem 7: 1-16 (1978) (5) Gschwend PM et al; Environ Sci Technol 16: 31-8 (1982) (6) Sauer TC Jr; Org Geochem 3: 91-101 (1981) (7) Mantoura RFC; Environ Sci Technol 16: 38-45 (1982) (8) Van de Meent D et al; Water Sci Technol 18: 73-81 (1986)]**PEER REVIEWED**

RAIN WATER: West Los Angeles, CA - 9 parts/trillion(1). Concn (parts/trillion) dissolved in rain, Portland, OR, Feb-April 1984, 7 rain events, 100% pos, 6.9-72, 34 avg(2).
[(1) Kawamura K, Kaplan IR; Environ Sci Technol 17: 497-501 (1983) (2) Ligocki MP; Atmos Environ 19: 1609-17 (1985)]**PEER REVIEWED**

Effluent Concentrations:

Industries with mean raw wastewater concentrations >2000 ppb: gum and wood chemicals (11,000 ppb), pharmaceutical manufacturing (10,000 ppb), paint and ink formulation, and auto and other laundries(1). Effluents from representative water treatment plants in Southern California were variable <10 ppb at San Diego City to 130 ppb at Los Angeles Co (both measurements following primary treatment)(2); <10 ppb detected following secondary treatment(2). In a US city survey, 17% of 6 samples were positive, 6.0 ppb avg(3), Lake Michigan, North Side sewage treatment plant - 1 ppb(4). USEPA STORET database, 1,368 data points, 7.4% pos, <3.0 ppb median(5). MN municipal solid waste landfills, leachates, 6 sites, 100% pos, 12-820 ppb, contaminated groundwater (by inorganic indices), 13 sites, 61.5% pos, 1.2-590 ppb, other groundwater (apparently not contaminated as indicated by inorganic indices), 7 sites, 14.3% pos, 9.4 ppb avg(6). 18.0 and 12.28 kilotons of ethylbenzene was emitted as part of gasoline exhaust emissions from motor vehicles in 1987 and 1990, respectively in UK(7).
[(1) USEPA; Treatability Manual p.I.9.8-3 USEPA 600/2-82-001a (1981) (2) Young DR; 1978 Ann Rep Southern Calif Coastal Water Res Proj p 103-12 (1978) (3) Callahan MA et al; p 55-61 in 8th Natl Conf Munic Sludge Manage Proc (1979) (4) Konasewich D et al; Status Report on Organic and Heavy Metal Contaminants in Lakes Erie, Michigan, Huron and Superior basins. Great Lakes Qual Board 373 p (1979) (5) Staples CA et al; Environ Toxicol Chem 4: 131-42 (1985) (6) Sabel GV, Clark TP; Waste Manag Res 2: 119-30 (1984) (7) Field, RA et al; Atmos Environ 26A: 2983-96 (1992)]**PEER REVIEWED**

Sediment/Soil Concentrations:

SOIL: Ethylbenzene concns found in three leachate samples taken from German hazardous waste sites where leachate samples A and B were both anaerobic and alkaline and leachate sample C was aerobic and slightly acidic, were 10, 3200, and 20,000 ug/l, respectively(1). SEDIMENTS: Sediments from the lower Tennessee River below Calvert City, KY measured 4.0 ppb for ethylbenzene(2). According to the USEPA STORET database, 350 data points were tested for ethylbenzene with 11% pos, 5.0 ppm median, dry weight(3).
[(1) Brack W et al; Environ Toxicol Chem 17: 1982-91 (1998) (2) Goodley PC, Gordon M; Kentucky Acad Sci 37: 11-5 (1976) (3) Staples CA et al; Environ Technol Chem 4: 131-42 (1985)]**PEER REVIEWED**

Atmospheric Concentrations:

SOURCE DOMINATED: The ethylbenzene concn measured 0.5-2.6 ppb in the Allegheny Mt. Tunnel, with concns directly corresponding to the number of vehicles passing through the tunnel(1). Emissions testing from motor vehicle traffic in a Los Angeles roadway tunnel showed concns of 143 mg/l of ethylbenzene(2). The Maastunnel in the Netherlands measured an avg ethylbenzene concn of 6 ppb(3). Concn (ppb) a rural motorway in UK, May-Aug 1983, 184 samples, not detected-1.14, 0.17 avg(4); Aug 1982, not detected-0.70, 0.25 avg(5). Ethylbenzene ambient air concns at 2 landfill sites in Ireland were found to have a min and max of 0.03 and 5.9, median of 0.8 ug/cu m (site with no leachate collection), and 0.03 and 47.6, median of 5.3 ug/cu m (site with leachate collection), respectively(6). Houston, TX 21 individuals in urban sites reported a range of 2.5 to 154.2 ppb(8). A natural gas facility in Rio Blanco County, CO measured 3.6 ppb, and a Texaco refinery in Tulsa, OK ranged from 4.7 to 7.9 ppb(7).

England - car park - 115 ppb, motorway - 92 ppb(9), while 6 sites at Gatwick airport ranged from 0.46 to 1.8 ppb, 1.4 ppb avg(10). 181 samples of US source dominated areas - 0.63 ppb avg(11).
[(1) Hampton CV et al; Environ Sci Technol 17: 699-708 (1983) (2) Fraser MP et al; Environ Sci Technol 32: 2051-60 (1998) (3) Bos R et al; Sci Total Environ 7: 269-81 (1977) (4) Clark AI et al; Sci Total Environ 39: 265-79 (1984) (5) Clark AI et al; Environ Pollut (Series B) 7: 141-58 (1984) (6) James KJ, Stack MA; Chemosphere 34: 1713-21 (1997) (7) Arnts RR, Meeks SA; Biogenic Hydrocarbon Contribution to the Ambient Air of Selected Areas 31 p USEPA 600/3-80-023 (1980) (8) Lonneman WA et al; Hydrocarbons in Houston air. USEPA 600/3-79-018 pp. 44 (1979) (9) Perry R, Twibell JD; Atmos Environ 7: 329-37 (1973) (10) Tsani-Bazaca E et al; Chemosphere 11: 11-23 (1982) (11) Brodzinsky R, Singh HB; Volatile Organic Chemicals in the Atmosphere: An Assessment of Available Data. SRI Contract 68-02-3452 pp. 198 (1982)]**PEER REVIEWED**

URBAN/SUBURBAN: Values for major western US cities ranged from 0.1 to 27.7 ppb(1,5,6,7,13), with the avg being 2.68 ppb(SRC). Representative centers in New Jersey had a range of 0.17 to 0.33 ppb avg, 107 of 110 samples pos(4). Ethylbenzene was detected but not quantified in another New Jersey study(11). It has been detected in 6 USSR cities, including Lenningrad as well as New York and Paris(8-10). The Hague, Netherlands - 5 ppb(2); Sidney Australia - 1.3 ppb(12); Japan - 0.2 ppb and Frankfurt-am-Main, Germany - 1 ppb(14). 3 sites in England away from traffic - 16.1 to 18.8 parts/trillion avg, 2 sites with heavy traffic 28.7 to 33.9 parts/trillion avg(3). 8.7 ppb measured in the atmosphere of Zurich, Switzerland(17). 669 samples from the US had a median concn of 1.2 ppb(15). 36 Chicago metropolitan area homes tested - 36% in outdoor air(16). Gas-phase concn (ng/cu m) during 7 rain events, Portland, OR, Feb-Apri 1984, 7 rain events 100% pos, 780-2800, 1300 avg(20). Concn (ppb), Exhibition Road, London, May-Aug 1983, 267 samples, 100% pos, 0.05-2.17, 0.78 avg(18); June-July 1982, 256 samples, not detected-3.3, 0.88 avg(19). US 1979-1984, 15 cities, 1-2 weeks of sampling/site, overall range, not detected-31.5 ppb; range of avg, 0.6-4-6 ppb, avg of avg, 1.9 ppb(21). Ethylbenzene outdoor air concns in Rio de Janeiro, Brazil ranged from 3.1-7.4 ug/cu m(22).
[(1) Arnts RR, Meeks SA; Biogenic Hydrocarbon Contribution to the Ambient Air of Selected Areas. pp. 31 USEPA 600/3-80-023 (1980) (2) Bos R et al; Sci Total Environ 7: 269-81 (1977) (3) Thornburn S, Colenutt BA; Int J Environ Stud 13: 265-71 (1979) (4) Harkov R et al; J Air Pollut Control Assoc 33: 1177-83 (1983) (5) Altshuller AP et al; Environ Sci Technol 5: 1009-16 (1971) (6) Lonneman WA et al; Environ Sci Technol 2: 1017-20 (1968) (7) Singh HB et al; Atmos Environ 15: 601-12 (1981) (8) Ioffe BV et al; Dokl Akad Nauk SSSR 243: 1186-9 (1978) (9) Ioffe BV et al; Environ Sci Technol 13: 864-8 (1979) (10) Ioffe BV et al; J Chromatogr 142: 787-95 (1977) (11) Lioy P et al; J Water Pollut Control Fed 33: 649-57 (1983) (12) Nelson PF, Quigley SM; Atmos Environ 17: 659-62 (1983) (13) Singh HB et al; Atmospheric Measurements of Selected Toxic Organic Chemicals. USEPA 600/3-80-072 (1980) (14) Santodonato J et al; Investigation of Selected Potential Environmental Contaminants; Styrene, Ethyl Benzene and Related Compounds. pp. 261 USEPA 560/11-80-018 (1980) (15) Brodzinsky R, Singh

HB; Volatile Organic Chemicals in the Atmosphere: An Assessment of Available Data 198 p SRI Contract 68-02-3452 (1982) (16) Jarke FH et al; ASHRAE Trans 87: 153-66 (1981) (17) Grob K, Grob g; J Chromatogr 62: 1-13 (1971) (18) Clark AI et al; Sci Total Environ 39: 265-79 (1984) (19) Clark AI et al; Environ Pollut (Series B) 7: 141-58 (1984) (20) Ligocki MP et al; Atmos Environ 19: 1609-17 (1985) (21) Singh HB et al; Atmos Environ 19: 1911-9 (1985) (22) Brickus LSR et al; Environ Sci Technol 32: 3485-90 (1998)]**PEER REVIEWED**

RURAL/REMOTE: Concentration in air sampls from rural and remote areas in the continental US ranged between 0.5 to 2.2 ppb(1,6). Samples from the Jones State Forest north of Houston, TX ranged from 0.8 to 10.4 ppb(3). Air intake in fan rooms of the Allegheny Mt. tunnel measured 0.07 to 0.16 ppb(2). Air samples in England - 11.3 parts/trillion avg(4); the Netherlands - 0.8 ppb avg; and Belgium 0.01 to 15 ppb(5). Concn at rural site in the UK, May-Aug 1983, 204 samples, not detected-0.70, 0.14 ppb avg(7); July 1982, 175 samples, not detected-0.6, 0.12 ppb avg(8).
[(1) Arnts RR, Meeks SA; Biogenic Hydrocarbon Contribution to the Ambient Air of Selected Areas. USEPA 600/3-80-023 pp. 31 (1980) (2) Hampton CV et al; Environ Sci Technol 17: 699-708 (1983) (3) Seila RL; Non-Urban Hydrocarbon Concentrations in Ambient Air North of Houston, TX. USEPA 500/3-79-010 pp. 38 (1979) (4) Thornburn S, Colenutt BA; Int J Environ Stud 13: 265-71 (1979) (5) Termonia M; pp. 356-61 in Comm Eur Comm EUR7624 Phys Chem Behav Atmos Pollut (1982) (6) Brodzinsky R, Singh HB; Volatile Organic Chemicals in the Atmosphere: An Assessment of Available Data. SRI Contract 68-02-3452 pp. 198 (1982) (7) Clark AI et al; Sci Total Environ 39: 265-79 (1984) (8) Clark AI et al; Environ Pollut (Series B) 7: 141-58 (1984)]**PEER REVIEWED**

RURAL/REMOTE: Between May-Aug 1983, 204 samples of air were tested for ethylbenzene at a rural site in UK and it was found that the sample concn ranged between not detected to 0.70 ppb, with an avg of 0.14 ppb(1). In July 1982, 175 samples from rural UK ranged between not detected to 0.6 ppb, with an avg of 0.12 ppb(2).
[(1) Clark AI et al; Sci Total Environ 39: 265-79 (1984) (2) Clark AI et al; Environ Pollut (Series B) 7: 141-58 (1984)]**PEER REVIEWED**

INDOOR: Ethylbenzene indoor air concns in Rio de Janeiro, Brazil ranged from 9.3-13.1 ug/cu m. samples from 36 Chicago metropolitan area homes tested showed a 57% detection frequency in indoor air(2).
[(1) Brickus LSR et al; Environ Sci Technol 32: 3485-90 (1998) (2) Jarke FH et al; ASHRAE Trans 87: 153-66 (1981)]**PEER REVIEWED**

Food Survey Values:

Ethylbenzene concns in supermarket eggs packed in polystyrene, fresh unpacked eggs, and fresh eggs packed in polystyrene were found to be 28, 4, and 4 ng/g, respectively(1). Duck meat, duck fat, cantonese style roasted duck, and cantonese style roasted duck gravy had concns of 0.47, 2.55, 4.07, and 12.30 ppb ethylbenzene, respectively(2). Ethylbenzene was detected but not quantified in mountain Beaufort cheese(3). Ethylbenzene was detected in dried legumes such as beans with a 5 ppb avg concn,

in split peas at 13 ppb, and in lentils at a 5 ppb concn(4).
[(1) Matiella JE, Hsieh TCKY; J Food Sci 56: 387-90 (1991) (2) Wu CM, Liou SE; J Agric Food Chem 40: 838-41 (1992) (3) Dumont JP, Adda J; J Agric Food Chem 26: 364-7 (1978) (4) Lovegren NV et al; J Agric Food Chem 27: 851-3 (1979)]**PEER REVIEWED**

Fish/Seafood Concentrations:

In 1982, bottomfish (sole and flounder species) from Commencement Bay and adjacent waterways in Tacoma, WA were found to have an avg concn of ethylbenzene of 0.01 ppm(1). 5 samples of oysters in Lake Pontchartrain, LA, had an avg concn of 0.8 ppb(2).
[(1) Nicola RM; J Environ Health 49: 342-7 (1987) (2) Ferrario JB et al; Bull Environ Contam Toxicol 34: 246-55 (1985)]**PEER REVIEWED**

Milk Concentrations:

Ethylbenzene was detected, but not quantified, in 8 of 8 samples of mother's milk from 4 US urban areas(1).
[(1) Pellizzari ED et al; Bull Environ Contam Toxicol 28: 322-8 (1982)]**PEER REVIEWED**

Other Environmental Concentrations:

Detected in cigarette smoke(1).
[(1) NAS; The Alkylbenzenes USEPA Contract No. 68-01-4655 (1980)]**PEER REVIEWED**

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Environmental Fate/Exposure Summary:

Ethylbenzene's production and use as an intermediate for the production of styrene, its presence in automotive and aviation fuels, and its presence in crude oil may result in its release to the environment through various waste streams. If released to air, a vapor pressure of 9.6 mm Hg at 25 deg C indicates ethylbenzene will exist solely as a vapor in the ambient atmosphere. Vapor-phase ethylbenzene will be degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals; the half-life for this reaction in air is estimated to be 55 hr. If released to soil, ethylbenzene is expected to have moderate mobility based upon an estimated Koc of 520. Volatilization from moist soil surfaces is expected to be an important fate process based upon a Henry's Law constant of 7.88X10-3 atm-cu m/mole. Ethylbenzene may volatilize from dry soil surfaces based upon its vapor pressure. Biodegradation in soil takes place via nitrate-reducing processes. If released into water, ethylbenzene may adsorb to suspended solids and sediment in water based upon the estimated Koc. Biodegradation in a gasoline contaminated aquifer ranged from 10-16 days under aerobic conditions. Ethylbenzene was degraded in 8 days in groundwater and 10 days in seawater as a component of gas oil. Volatilization from water surfaces is expected to be an important fate process based upon this compound's Henry's Law constant. Estimated volatilization half-lives for a model river and model lake are 1.1 and 99 hrs, respectively. Measured BCFs of 0.67 to 15 suggest the potential for bioconcentration in aquatic organisms is low. Hydrolysis is not expected to occur due to the lack of hydrolyzable functional groups. Occupational exposure to ethylbenzene may occur through inhalation at municipal waste composting facilities and via inhalation and dermal contact with this compound at workplaces where ethylbenzene is produced or used. The general population may be exposed to ethylbenzene via inhalation of ambient air, drinking and eating contaminated foods and water, and by handling gasoline. Ethylbenzene is likely to be detected in groundwater. (SRC)

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Natural Pollution Sources:

Ethylbenzene is a product of biomass combustion(1), and a component of crude oil(2).
[(1) Graedel TE; Atmospheric Chemical Compounds. New York NY Academic Press (1986) (2) Nunes P, Benville PE JR; Bull Environ Contam Toxicol 21: 71-24 (1979)]**PEER REVIEWED**

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Artificial Pollution Sources:

Ethylbenzene is present at 0.02 wt% in coke-oven tars.
[Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984.,p. V22 572 (1983)]**PEER REVIEWED**

Ethylbenzene's production and use as an intermediate for the manufacture of styrene and use as a resin solvent(1), intermediate for the production of diethylbenzene and acetophenone(2), and its use as a component of automotive and aviation fuels(3) may result in its release to the environment through various waste streams.
[(1) Budavari S, ed; The Merck Index. 12th ed. Whitehouse Station, NJ: Merck and Co., Inc. p. 643 (1996) (2) Coty RR et al; Ullmann's Encycl Indust Chem. 5th ed. Deerfield Beach, FL: VCH Pub A 10: 35-43 (1985) (3) Clayton GB, Clayton FE; Patty's Industrial Hygiene and Toxicology. 2B: Toxicology. 4th ed. NY, NY: John Wiley & Sons Inc 2B: 1342 (1994)]**PEER REVIEWED**

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Environmental Fate:

TERRESTRIAL FATE: Based on a classification scheme(1), an estimated Koc value of 520(SRC), determined from a structure estimation method(2), indicates that ethylbenzene is expected to have moderate mobility in soil(SRC). Volatilization of ethylbenzene from moist soil surfaces is expected to be an important fate process(SRC) given a Henry's Law constant of 7.88X10-3 atm-cu m/mole(3). The potential for volatilization of ethylbenzene from dry soil surfaces may exist(SRC) based upon a vapor pressure of 9.6 mm Hg(4). Ethylbenzene was completely degraded in microcosms inoculated with the sediment material from a refinery pond or activated sludge from the refinery treatment facility under nitrate-reducing conditions(5). At Sleeping Bear Dunes National Lakeshore in Michigan, ethylbenzene was degraded at slow rates via anaerobic degradation under ambient subsurface conditions using ferric iron, sulfate and/or carbon dioxide as the terminal electron acceptors(6).
[(1) Swann RL et al; Res Rev 85: 17-28 (1983) (2) Meylan WM et al; Environ Sci Technol 26: 1560-67 (1992) (3) Sanemasa I et al; Bull Chem Soc Japan 55: 1054-62 (1982) (4) Daubert TE et al; Physical and Thermodynamic Properties of Pure Chemicals. NY, NY: Hemisphere Pub Corp (1989) (5) Ball HA et al; pp. 458-63 in In-Situ Bioreclamation. Hinchee RE, Olfenbuttel RF, eds. Boston, MA: Butterworth-Heinemann (1991) (6) Borden RC et al; Anaerobic biodegradation of BTEX in aquifer material. USEPA/600/S-97/003 pp. 9 (1997)]**PEER REVIEWED**

AQUATIC FATE: Based on a classification scheme(1), an estimated Koc value of 520(SRC), determined from an estimation method(2), indicates that ethylbenzene may adsorb to suspended solids and sediment(SRC). Volatilization from water surfaces is expected(3) based upon a Henry's Law constant of 7.88X10-3 atm-cu m/mole(4). Using this Henry's Law constant and an estimation method(3), volatilization half-lives for a model river and model lake are 1.1 and 99 hr, respectively(SRC). According to a classification scheme(5), an experimental log BCF of 1.19(7), which corresponds to a BCF of 15, suggests the potential for bioconcentration in aquatic organisms is low. In a shallow coastal plain aquifer contaminated with gasoline and diesel fuel in rural Sampson County in North Carolina, ethylbenzene was degraded in aerobic conditions within 10-16 days and in conditions of low initial oxygen, it was rapidly degraded in 21 days until the available oxygen was depleted(8). As a component of gas oil, ethylbenzene is completely degraded in groundwater in 8 days(9) and seawater in 10 days(10). In a mesocosm experiment using simulated Narragansett Bay conditions, complete biodegradation occurred in approximately 2 days after a 2 week lag in spring and a 2 day lag in summer(11).
[(1) Swann RL et al; Res Rev 85: 17-28 (1983) (2) Meylan WM et al; Environ Sci Technol 26: 1560-67 (1992) (3) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington, DC: Amer Chem Soc pp. 4-9, 15-1 to 15-29 (1990) (4) Sanemasa I et al; Bull Chem Soc Japan 55: 1054-62 (1982) (5) France C et al; Chemosphere 29: 1501-14 (1994) (6) Hansch C et al; Exploring QSAR. Hydrophobic, Electronic, and Steric Constants. ACS Prof Ref Book. Heller SR, consult. ed., Washington, DC: Amer Chem Soc p. 43 (1995) (7) Park JH, Lee HJ;

Chemosphere 26: 1905-16 (1993) (8) Borden RC et al; Water Resour Res 33: 1105-15 (1996) (9) Kappeler T, Wuhrmann K; Water Res 12: 327-33 (1978) (10) Van der Linden AC; Dev Biodegrad Hydrocarbons 1: 165-200 (1978) (11) Wakeham SG et al; Environ Sci Technol 17: 611-7 (1983)]**PEER REVIEWED**

ATMOSPHERIC FATE: According to a model of gas/particle partitioning of semivolatile organic compounds in the atmosphere(1), ethylbenzene, which has a vapor pressure of 9.6 mm Hg at 25 deg C(2), is expected to exist solely as a vapor. Vapor-phase ethylbenzene is degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals(SRC); the half-life for this reaction in air is 55 hr(SRC), calculated from its rate constant of 7.1X10-12 cu cm/molecule-sec at 25 deg C(3).
[(1) Bidleman TF; Environ Sci Technol 22: 361-367 (1988) (2) Daubert TE et al; Physical & Thermodynamic Properties of Pure Chemicals NY, NY: Hemisphere Pub Corp (1989) (3) Atkinson R; J Phys Chem Ref Data Monograph No. 2 p. 48 (1994)]**PEER REVIEWED**

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Environmental Biodegradation:

After a period of inocula adaptation, ethylbenzene is biodegraded fairly rapidly by sewage or activated sludge inoculua(1-3,9). As a component of gas oil, it is completely degraded in groundwater in 8 days(4) and seawater in 10 days(5). In a mesocosm experiment using simulated Narragansett Bay conditions, complete biodegradation occurred in approximately 2 days after a 2 week lag in spring and a 2 day lag in summer(6). Part of the attenuation in concn from a leaky gasoline storage tank in the chalk aquifer in England has been attributed to biodegradation(7). No degradation was observed in an anaerobic reactor even after 110 days acclimation(8) or at low concentrations in a batch reactor in 11 weeks under denitrifying conditions(10). Percent removal in an anaerobic, continuous-flow, laboratory bioflim column was 7% after a 2 day detention time(11); 99% removal was observed in a similar aerobic column following a 20 min detention time(11).
[(1) Slave T et al; Rev Chim 25: 666-70 (1974) (2) Tabak HH et al; J Water Pollut Control Fed 53: 1503-18 (1981) (3) Malaney GW, McKinney RE; Water Sewage Works 113: 302-9 (1966) (4) Kappeler T, Wuhrmann K; Water Res 12: 327-33 (1978) (5) Van der Linden AC; Dev Biodegrad Hydrocarbons 1: 165-200 (1978) (6) Wakeham SG et al; Environ Sci Technol 17: 611-7 (1983) (7) Tester DJ, Harker RJ; Water Pollut Control 80: 614-31 (1981) (8) Chou WL et al; Biotechnol Bioeng Symp 8: 391-414 (1979) (9) USEPA; Treatability Manual p 1.9.8-1 to 1.9.8-5 USEPA 600/2-82-001a (1981) (10) Bouwer EJ, McCarty PL; Appl Environ Microbiol 45: 1295-99 (1983) (11) Bouwer EJ, McCarthy PL; Ground Water 22: 433-40 (1984)]**PEER REVIEWED**

AEROBIC: A study was conducted using underground storage tanks containing gasoline and diesel fuel that contaminated a shallow coastal plain aquifer in rural Sampson County in North Carolina. Ethylbenzene was degraded in aerobic conditions within 10-16 days and in conditions of low initial oxygen, it was rapidly degraded in 21 days until the available oxygen was depleted(1). A combined culture experiment of Mycobacterium vaccae and Rhodococcus sp. strain R-22 showed M. vaccae alone and M. vaccae and R-22 together can oxidize ethylbenzene to 4-ethylphenol which is then degraded to 50 ppm within 72 hr(2).
[(1) Borden RC et al; Water Resour Res 33: 1105-15 (1996) (2) Fairlee JR et al; J Microbiol 43: 841-6 (1997)]**PEER REVIEWED**

ANAEROBIC: Anaerobic ethylbenzene transformation in Seal Beach Naval Weapons Station sediments in Southern California appeared to be strictly associated with nitrate-reducing processes(1). Ethylbenzene was completely degraded in microcosms inoculated with the sediment material from a refinery pond or activated sludge from the refinery treatment facility under nitrate-reducing conditions(2). At Sleeping Bear Dunes National Lakeshore in Michigan, ethylbenzene was degraded at slow rates via anaerobic degradation under ambient subsurface conditions using ferric iron, sulfate and/or carbon dioxide as the terminal electron acceptors(3).
[(1) Ball HA, Reinhard M; Environ Toxicol Chem 15: 114-22 (1996) (2) Ball HA et al; pp. 458-63 in In-Situ Bioreclamation. Hinchee RE,

Olfenbuttel RF, eds. Boston, MA: Butterworth-Heinemann (1991) (3) Borden RC et al; Anaerobic biodegradation of BTEX in aquifer material. USEPA/600/S-97/003 pp. 9 (1997)]**PEER REVIEWED**

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Environmental Abiotic Degradation:

The rate constant for the vapor-phase reaction of ethylbenzene with photochemically-produced hydroxyl radicals is 7.1X10-12 cu cm/molecule-sec at 298 K(1) which corresponds to an atmospheric half-life of about 55 hr at an atmospheric concn of 5X10+5 hydroxyl radicals per cu cm. Ethylbenzene is not expected to undergo hydrolysis in the environment due to the lack of hydrolyzable functional groups(2). Ethylbenzene photolysis occurs via photooxidation hydrogen abstraction from the alkyl group by photooxydatively formed hydroxyl radical which results in the formation of acetophenone, and eventually benzaldehyde with 2-butanedial, 4-oxo-2-hexenal, and 2-ethyl-2-butenedial being suggested as further end products(3).
[(1) Atkinson R; J Phys Chem Ref Data Monograph No. 2 p. 48 (1994) (2) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington, DC: Amer Chem Soc pp. 7-4, 7-5 (1990) (3) Forstner HJL et al; Environ Sci Technol 31: 1345-58 (1997)]**PEER REVIEWED**

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Environmental Bioconcentration:

Experimental data on the bioconcentration of ethylbenzene include a log BCF of 1.9 in goldfish(2) and a log BCF of 0.67 for clams exposed to the water-soluble fraction of crude oil(1). Experimentally, a log BCF of 1.19 has also been reported(4) which corresponds to a BCF of 15. According to a classification scheme(3), these BCFs suggest the potential for bioconcentration in aquatic organisms is low.
[(1) Nunes P, Benville PE Jr; Bull Environ Contam Toxicol 21: 719-24 (1979) (2) Ogata M et al; Bull Environ Contam Toxicol 33: 561-7 (1984) (3) Franke C et al; Chemosphere 29: 1501-14 (1994) (4) Park JH, Lee HJ; Chemosphere 26: 1905-16 (1993)]**PEER REVIEWED**

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Soil Adsorption/Mobility:

Using a structure estimation method based on molecular connectivity indices(1), the Koc for ethylbenzene can be estimated to be 520(SRC). According to a classification scheme(2), this estimated Koc value suggests that ethylbenzene is expected to have low mobility in soil.

[(1) Meylan WM et al; Environ Sci Technol 26: 1560-67 (1992) (2) Swann RL et al; Res Rev 85: 17-28 (1983)]**PEER REVIEWED**

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Volatilization from Water/Soil:

The Henry's Law constant for ethylbenzene is 7.88X10-3 atm-cu m/mole(1). This Henry's Law constant indicates that ethylbenzene will volatilize from water surfaces(2). Based on this Henry's Law constant, the volatilization half-life from a model river (1 m deep, flowing 1 m/sec, wind velocity of 3 m/sec)(2) is estimated as 1.1 hr(SRC). The volatilization half-life from a model lake (1 m deep, flowing 0.05 m/sec, wind velocity of 0.5 m/sec)(2) is estimated as 99 hr(SRC). Ethylbenzene's Henry's Law constant(1) indicates that volatilization from moist soil surfaces may occur(SRC). The potential for volatilization of ethylbenzene from dry soil surfaces may exist(SRC) based upon a vapor pressure of 9.6 mm Hg(3). [(1) Sanemasa I et al; Bull Chem Soc Jpn 55: 1054-62 (1982) (2) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington, DC: Amer Chem Soc pp. 15-1 to 15-29 (1990) (3) Daubert TE et al; Physical & Thermodynamic Properties of Pure Chemicals NY, NY: Hemisphere Pub Corp (1989)]**PEER REVIEWED**

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Environmental Water Concentrations:

DRINKING WATER: In surveys of representative US municipal water supplies, ethylbenzene has been detected in most cases(1,2,4-8,10). Values for 3 New Orleans finished drinking waters ranged 1.6 to 2.3 ppb(6). Chicago Central Water Works on Lake Michigan measured 4 ppb(8). It has been found in the water supply for Evansville, IN on the Ohio River(7). 6 of 10 US cities were found to be positive(1,4). One US city had 1 of 4 samples pos with a 1 ppb avg, while another reported no positive samples(5). Tap water from bank infiltrated Rhine River water in the Netherlands measured 30 ppb in one study(3). Zurich, Switzerland tap water - detected not quantified(9). 1982 US groundwater supply survey, random samples of finished water supplies using groundwater as a source, 466 random samples, 0.6%, pos (0.5 ppb detection limit), 0.8 ppb median, 1.1 ppb max(10).
[(1) NAS; The Alkylbenzenes p III-13 Contract 68-01-4655 (1980) (2) Shackelford WM, Keith, LH; Frequency of Organic Compounds in Surface Waters USEPA 600/4-76-062 (1976) (3) Piet GJ, Morra CF; p 31-42 in Artificial Groundwater Recharge; Huisman L, Olsthorn TN, eds (1983) (4) Bedding ND et al; Sci Total Environ 25: 143-67 (1982) (5) Callahan MA et al; p 55-61 in 8th Natl Conf Munic Sludge Manage Proc (1979) (6) Keith, LH et al; p 329-73 in Identification and Analysis of Organic Pollutants in Water. Keith LH ed (1976) (7) Kleopfer RD, Fairless BJ; Environ Sci Technol 6: 1036-7 (1972) (8) Konasewich D et al; Status Report on Organic and Heavy Metal Contaminants in the Lakes Erie, Michigan, Huron and Superior Basins. Great Lakes Quality Review Board (1978) (9) Santodonato J et al; Investigation of selected potential environmental contaminants: styrene, ethylbenzene and related compounds 261 p USEPA 560/11-80-018 (1980) (10) Cotruvo JA; Sci Technol Environ 47: 7-26 (1985)]**PEER REVIEWED**

GROUNDWATER: A well in Ames, IA measured 15 ppb 50 yr after tar residues were buried at a nearby coal gas plant(5). Concns of 82-400 ppb were detected in two aquifers near the Hoe Creek underground coal gasification site in Wyoming, 15 mo after gasification was complete(2). In a US survey, 1970-76, it was detected but not quantified in well waters(1). In Jackson Township, NJ, drinking water wells measured 2000 ppb(4). Chalk aquifer in East Anglia, England - 210 m from petroleum storage - 0.15 ppb, 10 m distance - 1110 ppb, and 100-200 m - <250 ppb(3).
[(1) Shackelford WM, Keith, LH; Frequency of Organic Compounds Identified in Water USEPA 600/4-76-062 (1976) (2) Stuermer DH et al; Environ Sci Technol 16: 582-7 (1982) (3) Tester DH, Harker RJ; Water Pollut Control 80: 614-31 (1981) (4) Burmaster DE; Environ 24: 6-13, 33-6 (1982) (5) Santodonato J et al; Investigation of Selected Potential Environmental Contaminants: Styrene, Ethylbenzene and Related Compounds 261 p USEPA 560/11-80-018 (1980)]**PEER REVIEWED**

SURFACE WATER: Ethylbenzene has been detected but not quantified in a 1970-76 US survey(1,4). 14 heavily industrialized US river basins, 5 of 204 sites pos - 1-4 ppb; Chicago area and Illinois River Basin,

5 of 31 sites pos - 1-4 ppb(6). Two representative US cities, city A - 41% of 28 samples pos, 5.0 ppb avg, city B - 40% of 48 samples pos 3.2 ppb avg(2). Lower Tennessee River near Calvert City, KY reported 4.0 ppb(7). Lake Michigan, Chicago Sanitary and Ship Channel measured 1-2 ppb(3). River Glatt, Switzerland -detected, not quantified(5). USEPA STORET database, 1,101 data points, 10% pos, <5.0 ppb median(8).
[(1) Shackelford WM, Keith LH; Frequency of Organic Compounds Identified in Water USEPA 600/4-76-062 (1976) (2) Callahan MA et al; p 55-61 in 8th Natl Conf Munic Sludge Manage Proc (1979) (3) Konasewich D et al; Status Report on Organic and Heavy Metal Contaminants in the Lakes Erie, Michigan, Huron and Superior Basins. Great Lakes Quality Review Board (1978) (4) Bertsch W et al; J Chromatogr 112: 701-18 (1975) (5) Zuercher F, Giger W; Vom Wasser 47: 37-55 (1976) (6) Ewing BB et al; Monitoring to Detect Previously Unrecognized Pollutants in Surface Waters 75 p USEPA 560/6-77-015 (appendix USEPA 560/6-77-015a) (1977) (7) Goodley PG, Gordon M; Kentucky Acad Sci 37: 11-5 (1976) (8) Staples CA et al; Environ Toxicol Chem 4: 131-42 (1985)]**PEER REVIEWED**

SEAWATER: Ethylbenzene concns were found to be 30-50 ng/l in an estuary in Brazos, US; between <10-46.3 ng/l in UK; and 36.9 ng/l in Belgium(1). Ethylbenzene has been found in concns of 4.5-30 ng/l in Vineyard Sound; 0.4-4.5 ng/l in coastal and shelf sea water in the Gulf of Mexico; 5.5-22 ng/l in the coastal waters of Spain; 4.3-380 ng/l in Campeche Shelf; <10 ng/l in shelf and bay waters in UK; and 9.4-18.7 ng/l in Belgian Continental Shelf(1). Ethylbenzene mean concn of 21.94 ng/l was found in the South Northern sea up to 60 km offshore in the Scheldt Estuary(2). In the coastal waters off the western Gulf of Mexico at the mouth of the Brazos River, TX, ethylbenzene concns range between 0.004-0.5 ug/l(3). In the Gulf of Mexico in unpolluted areas ethylbenzene concn is 0.4 to 5 ppb(4,6), while an area of anthropogenic influence ranged from 5 to 15 ppb(6). Cape Cod, MA measured ethylbenzene at 22 ppb(5,7) with 11 ppb being avg(5). In the coastal waters of the Dutch Northern Sea, 108 samples ranged from not detected to 20 parts per trillion and averaged 4 parts per trillion(8).
[(1) Dewulf J, Vanlangenhove H; Water Res 31: 1825-38 (1997) (2) Dewulf JP et al; Environ Sci Technol 32: 903-11 (1998) (3) Neff JM, Sauer TC Jr; Environ Sci Res 52: 163-75 (1996)(4) Sauer TC Jr et al; Mar Chem 7: 1-16 (1978) (5) Gschwend PM et al; Environ Sci Technol 16: 31-8 (1982) (6) Sauer TC Jr; Org Geochem 3: 91-101 (1981) (7) Mantoura RFC; Environ Sci Technol 16: 38-45 (1982) (8) Van de Meent D et al; Water Sci Technol 18: 73-81 (1986)]**PEER REVIEWED**

RAIN WATER: West Los Angeles, CA - 9 parts/trillion(1). Concn (parts/trillion) dissolved in rain, Portland, OR, Feb-April 1984, 7 rain events, 100% pos, 6.9-72, 34 avg(2).
[(1) Kawamura K, Kaplan IR; Environ Sci Technol 17: 497-501 (1983) (2) Ligocki MP; Atmos Environ 19: 1609-17 (1985)]**PEER REVIEWED**

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Effluent Concentrations:

Industries with mean raw wastewater concentrations >2000 ppb: gum and wood chemicals (11,000 ppb), pharmaceutical manufacturing (10,000 ppb), paint and ink formulation, and auto and other laundries(1). Effluents from representative water treatment plants in Southern California were variable <10 ppb at San Diego City to 130 ppb at Los Angeles Co (both measurements following primary treatment)(2); <10 ppb detected following secondary treatment(2). In a US city survey, 17% of 6 samples were positive, 6.0 ppb avg(3), Lake Michigan, North Side sewage treatment plant - 1 ppb(4). USEPA STORET database, 1,368 data points, 7.4% pos, <3.0 ppb median(5). MN municipal solid waste landfills, leachates, 6 sites, 100% pos, 12-820 ppb, contaminated groundwater (by inorganic indices), 13 sites, 61.5% pos, 1.2-590 ppb, other groundwater (apparently not contaminated as indicated by inorganic indices), 7 sites, 14.3% pos, 9.4 ppb avg(6). 18.0 and 12.28 kilotons of ethylbenzene was emitted as part of gasoline exhaust emissions from motor vehicles in 1987 and 1990, respectively in UK(7).

[(1) USEPA; Treatability Manual p.I.9.8-3 USEPA 600/2-82-001a (1981) (2) Young DR; 1978 Ann Rep Southern Calif Coastal Water Res Proj p 103-12 (1978) (3) Callahan MA et al; p 55-61 in 8th Natl Conf Munic Sludge Manage Proc (1979) (4) Konasewich D et al; Status Report on Organic and Heavy Metal Contaminants in Lakes Erie, Michigan, Huron and Superior basins. Great Lakes Qual Board 373 p (1979) (5) Staples CA et al; Environ Toxicol Chem 4: 131-42 (1985) (6) Sabel GV, Clark TP; Waste Manag Res 2: 119-30 (1984) (7) Field, RA et al; Atmos Environ 26A: 2983-96 (1992)]**PEER REVIEWED**

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Sediment/Soil Concentrations:

SOIL: Ethylbenzene concns found in three leachate samples taken from German hazardous waste sites where leachate samples A and B were both anaerobic and alkaline and leachate sample C was aerobic and slightly acidic, were 10, 3200, and 20,000 ug/l, respectively(1). SEDIMENTS: Sediments from the lower Tennessee River below Calvert City, KY measured 4.0 ppb for ethylbenzene(2). According to the USEPA STORET database, 350 data points were tested for ethylbenzene with 11% pos, 5.0 ppm median, dry weight(3).

[(1) Brack W et al; Environ Toxicol Chem 17: 1982-91 (1998) (2) Goodley PC, Gordon M; Kentucky Acad Sci 37: 11-5 (1976) (3) Staples CA et al; Environ Technol Chem 4: 131-42 (1985)]**PEER REVIEWED**

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Atmospheric Concentrations:

SOURCE DOMINATED: The ethylbenzene concn measured 0.5-2.6 ppb in the Allegheny Mt. Tunnel, with concns directly corresponding to the number of vehicles passing through the tunnel(1). Emissions testing from motor vehicle traffic in a Los Angeles roadway tunnel showed concns of 143 mg/l of ethylbenzene(2). The Maastunnel in the Netherlands measured an avg ethylbenzene concn of 6 ppb(3). Concn (ppb) a rural motorway in UK, May-Aug 1983, 184 samples, not detected-1.14, 0.17 avg(4); Aug 1982, not detected-0.70, 0.25 avg(5). Ethylbenzene ambient air concns at 2 landfill sites in Ireland were found to have a min and max of 0.03 and 5.9, median of 0.8 ug/cu m (site with no leachate collection), and 0.03 and 47.6, median of 5.3 ug/cu m (site with leachate collection), respectively(6). Houston, TX 21 individuals in urban sites reported a range of 2.5 to 154.2 ppb(8). A natural gas facility in Rio Blanco County, CO measured 3.6 ppb, and a Texaco refinery in Tulsa, OK ranged from 4.7 to 7.9 ppb(7). England - car park - 115 ppb, motorway - 92 ppb(9), while 6 sites at Gatwick airport ranged from 0.46 to 1.8 ppb, 1.4 ppb avg(10). 181 samples of US source dominated areas - 0.63 ppb avg(11). [(1) Hampton CV et al; Environ Sci Technol 17: 699-708 (1983) (2) Fraser MP et al; Environ Sci Technol 32: 2051-60 (1998) (3) Bos R et al; Sci Total Environ 7: 269-81 (1977) (4) Clark AI et al; Sci Total Environ 39: 265-79 (1984) (5) Clark AI et al; Environ Pollut (Series B) 7: 141-58 (1984) (6) James KJ, Stack MA; Chemosphere 34: 1713-21 (1997) (7) Arnts RR, Meeks SA; Biogenic Hydrocarbon Contribution to the Ambient Air of Selected Areas 31 p USEPA 600/3-80-023 (1980) (8) Lonneman WA et al; Hydrocarbons in Houston air. USEPA 600/3-79-018 pp. 44 (1979) (9) Perry R, Twibell JD; Atmos Environ 7: 329-37 (1973) (10) Tsani-Bazaca E et al; Chemosphere 11: 11-23 (1982) (11) Brodzinsky R, Singh HB; Volatile Organic Chemicals in the Atmosphere: An Assessment of Available Data. SRI Contract 68-02-3452 pp. 198 (1982)]**PEER REVIEWED**

URBAN/SUBURBAN: Values for major western US cities ranged from 0.1 to 27.7 ppb(1,5,6,7,13), with the avg being 2.68 ppb(SRC). Representative centers in New Jersey had a range of 0.17 to 0.33 ppb avg, 107 of 110 samples pos(4). Ethylbenzene was detected but not quantified in another New Jersey study(11). It has been detected in 6 USSR cities, including Lenningrad as well as New York and Paris(8-10). The Hague, Netherlands - 5 ppb(2); Sidney Australia - 1.3 ppb(12); Japan - 0.2 ppb and Frankfurt-am-Main, Germany - 1 ppb(14). 3 sites in England away from traffic - 16.1 to 18.8 parts/trillion avg, 2 sites with heavy traffic 28.7 to 33.9 parts/trillion avg(3). 8.7 ppb measured in the atmosphere of Zurich, Switzerland(17). 669 samples from the US had a median concn of 1.2 ppb(15). 36 Chicago metropolitan area homes tested - 36% in outdoor air(16). Gas-phase concn (ng/cu m) during 7 rain events, Portland, OR, Feb-Apri 1984, 7 rain events 100% pos, 780-2800, 1300 avg(20). Concn (ppb), Exhibition Road, London, May-Aug 1983, 267 samples, 100% pos, 0.05-2.17, 0.78 avg(18); June-July 1982, 256 samples, not detected-3.3, 0.88 avg(19). US 1979-1984, 15 cities, 1-2 weeks of sampling/site, overall range, not detected-31.5 ppb; range of avg, 0.6-4-6 ppb, avg of avg, 1.9 ppb(21). Ethylbenzene outdoor air concns in Rio de Janeiro, Brazil ranged from 3.1-7.4 ug/cu m(22).

[(1) Arnts RR, Meeks SA; Biogenic Hydrocarbon Contribution to the Ambient Air of Selected Areas. pp. 31 USEPA 600/3-80-023 (1980) (2) Bos R et al; Sci Total Environ 7: 269-81 (1977) (3) Thornburn S, Colenutt BA; Int J Environ Stud 13: 265-71 (1979) (4) Harkov R et al; J Air Pollut Control Assoc 33: 1177-83 (1983) (5) Altshuller AP et al; Environ Sci Technol 5: 1009-16 (1971) (6) Lonneman WA et al; Environ Sci Technol 2: 1017-20 (1968) (7) Singh HB et al; Atmos Environ 15: 601-12 (1981) (8) Ioffe BV et al; Dokl Akad Nauk SSSR 243: 1186-9 (1978) (9) Ioffe BV et al; Environ Sci Technol 13: 864-8 (1979) (10) Ioffe BV et al; J Chromatogr 142: 787-95 (1977) (11) Lioy P et al; J Water Pollut Control Fed 33: 649-57 (1983) (12) Nelson PF, Quigley SM; Atmos Environ 17: 659-62 (1983) (13) Singh HB et al; Atmospheric Measurements of Selected Toxic Organic Chemicals. USEPA 600/3-80-072 (1980) (14) Santodonato J et al; Investigation of Selected Potential Environmental Contaminants; Styrene, Ethyl Benzene and Related Compounds. pp. 261 USEPA 560/11-80-018 (1980) (15) Brodzinsky R, Singh HB; Volatile Organic Chemicals in the Atmosphere: An Assessment of Available Data 198 p SRI Contract 68-02-3452 (1982) (16) Jarke FH et al; ASHRAE Trans 87: 153-66 (1981) (17) Grob K, Grob g; J Chromatogr 62: 1-13 (1971) (18) Clark AI et al; Sci Total Environ 39: 265-79 (1984) (19) Clark AI et al; Environ Pollut (Series B) 7: 141-58 (1984) (20) Ligocki MP et al; Atmos Environ 19: 1609-17 (1985) (21) Singh HB et al; Atmos Environ 19: 1911-9 (1985) (22) Brickus LSR et al; Environ Sci Technol 32: 3485-90 (1998)]**PEER REVIEWED**

RURAL/REMOTE: Concentration in air sampls from rural and remote areas in the continental US ranged between 0.5 to 2.2 ppb(1,6). Samples from the Jones State Forest north of Houston, TX ranged from 0.8 to 10.4 ppb(3). Air intake in fan rooms of the Allegheny Mt. tunnel measured 0.07 to 0.16 ppb(2). Air samples in England - 11.3 parts/trillion avg(4); the Netherlands - 0.8 ppb avg; and Belgium 0.01 to 15 ppb(5). Concn at rural site in the UK, May-Aug 1983, 204 samples, not detected-0.70, 0.14 ppb avg(7); July 1982, 175 samples, not detected-0.6, 0.12 ppb avg(8).
[(1) Arnts RR, Meeks SA; Biogenic Hydrocarbon Contribution to the Ambient Air of Selected Areas. USEPA 600/3-80-023 pp. 31 (1980) (2) Hampton CV et al; Environ Sci Technol 17: 699-708 (1983) (3) Seila RL; Non-Urban Hydrocarbon Concentrations in Ambient Air North of Houston, TX. USEPA 500/3-79-010 pp. 38 (1979) (4) Thornburn S, Colenutt BA; Int J Environ Stud 13: 265-71 (1979) (5) Termonia M; pp. 356-61 in Comm Eur Comm EUR7624 Phys Chem Behav Atmos Pollut (1982) (6) Brodzinsky R, Singh HB; Volatile Organic Chemicals in the Atmosphere: An Assessment of Available Data. SRI Contract 68-02-3452 pp. 198 (1982) (7) Clark AI et al; Sci Total Environ 39: 265-79 (1984) (8) Clark AI et al; Environ Pollut (Series B) 7: 141-58 (1984)]**PEER REVIEWED**

RURAL/REMOTE: Between May-Aug 1983, 204 samples of air were tested for ethylbenzene at a rural site in UK and it was found that the sample concn ranged between not detected to 0.70 ppb, with an avg of 0.14 ppb(1). In July 1982, 175 samples from rural UK ranged between not detected to 0.6 ppb, with an

avg of 0.12 ppb(2).
[(1) Clark AI et al; Sci Total Environ 39: 265-79 (1984) (2) Clark AI et al; Environ Pollut (Series B) 7: 141-58 (1984)]**PEER REVIEWED**

INDOOR: Ethylbenzene indoor air concns in Rio de Janeiro, Brazil ranged from 9.3-13.1 ug/cu m. samples from 36 Chicago metropolitan area homes tested showed a 57% detection frequency in indoor air(2).
[(1) Brickus LSR et al; Environ Sci Technol 32: 3485-90 (1998) (2) Jarke FH et al; ASHRAE Trans 87: 153-66 (1981)]**PEER REVIEWED**

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Food Survey Values:

Ethylbenzene concns in supermarket eggs packed in polystyrene, fresh unpacked eggs, and fresh eggs packed in polystyrene were found to be 28, 4, and 4 ng/g, respectively(1). Duck meat, duck fat, cantonese style roasted duck, and cantonese style roasted duck gravy had concns of 0.47, 2.55, 4.07, and 12.30 ppb ethylbenzene, respectively(2). Ethylbenzene was detected but not quantified in mountain Beaufort cheese(3). Ethylbenzene was detected in dried legumes such as beans with a 5 ppb avg concn, in split peas at 13 ppb, and in lentils at a 5 ppb concn(4).

[(1) Matiella JE, Hsieh TCKY; J Food Sci 56: 387-90 (1991) (2) Wu CM, Liou SE; J Agric Food Chem 40: 838-41 (1992) (3) Dumont JP, Adda J; J Agric Food Chem 26: 364-7 (1978) (4) Lovegren NV et al; J Agric Food Chem 27: 851-3 (1979)]**PEER REVIEWED**

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Fish/Seafood Concentrations:

In 1982, bottomfish (sole and flounder species) from Commencement Bay and adjacent waterways in Tacoma, WA were found to have an avg concn of ethylbenzene of 0.01 ppm(1). 5 samples of oysters in Lake Pontchartrain, LA, had an avg concn of 0.8 ppb(2).
[(1) Nicola RM; J Environ Health 49: 342-7 (1987) (2) Ferrario JB et al; Bull Environ Contam Toxicol 34: 246-55 (1985)]**PEER REVIEWED**

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Milk Concentrations:

Ethylbenzene was detected, but not quantified, in 8 of 8 samples of mother's milk from 4 US urban areas(1).

[(1) Pellizzari ED et al; Bull Environ Contam Toxicol 28: 322-8 (1982)]**PEER REVIEWED**

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Other Environmental Concentrations:

Detected in cigarette smoke(1).

[(1) NAS; The Alkylbenzenes USEPA Contract No. 68-01-4655 (1980)]**PEER REVIEWED**

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Environmental Standards & Regulations:

Acceptable Daily Intakes:

Acceptable daily intake: 1.6 mg/day
[USEPA; Ambient Water Quality Criteria Doc: Ethylbenzene p.C-22 (1980) EPA 440/5-80-048]**PEER REVIEWED**

TSCA Requirements:

Pursuant to section 8(d) of TSCA, EPA promulgated a model Health and Safety Data Reporting Rule. The section 8(d) model rule requires manufacturers, importers, and processors of listed chemical substances and mixtures to submit to EPA copies and lists of unpublished health and safety studies. Ethylbenzene is included on this list.
[40 CFR 716.120 (7/1/99)]**PEER REVIEWED**

CERCLA Reportable Quantities:

Persons in charge of vessels or facilities are required to notify the National Response Center (NRC) immediately, when there is a release of this designated hazardous substance, in an amount equal to or greater than its reportable quantity of 1000 lb or 454 kg. The toll free number of the NRC is (800) 424-8802; In the Washington D.C. metropolitan area (202) 426-2675. The rule for determining when notification is required is stated in 40 CFR 302.4 (section IV. D.3.b).
[40 CFR 302.4 (7/1/99)]**PEER REVIEWED**

RCRA Requirements:

F003; When ethylbenzene is a spent solvent, it is classified as a hazardous waste from a nonspecific source (F003), as stated in 40 CFR 261.31, and must be managed according to State and/or Federal hazardous waste regulations.
[40 CFR 261.31 (7/1/99)]**PEER REVIEWED**

Atmospheric Standards:

This action promulgates standards of performance for equipment leaks of Volatile Organic Compounds (VOC) in the Synthetic Organic Chemical Manufacturing Industry (SOCMI). The intended effect of these standards is to require all newly constructed, modified, and reconstructed SOCMI process units to use the best demonstrated system of continuous emission reduction for equipment leaks of VOC, considering costs, non air quality health and environmental impact and energy requirements. Ethylbenzene is produced, as an intermediate or a final product, by process units covered under this subpart.
[40 CFR 60.489 (7/1/99)]**PEER REVIEWED**

Listed as a hazardous air pollutant (HAP) generally known or suspected to cause serious health problems. The Clean Air Act, as amended in 1990, directs EPA to set standards requiring major sources to sharply

reduce routine emissions of toxic pollutants. EPA is required to establish and phase in specific performance based standards for all air emission sources that emit one or more of the listed pollutants. Ethylbenzene is included on this list.
[Clean Air Act as amended in 1990, Sect. 112 (b) (1) Public Law 101-549 Nov. 15, 1990]**PEER REVIEWED**

Clean Water Act Requirements:

Toxic pollutant designated pursuant to section 307(a)(1) of the Federal Water Pollution Control Act and is subject to effluent limitations.
[40 CFR 401.15 (7/1/99)] **QC REVIEWED**

Ethylbenzene is designated as a hazardous substance under section 311(b)(2)(A) of the Federal Water Pollution Control Act and further regulated by the Clean Water Act Amendments of 1977 and 1978. These regulations apply to discharges of this substance. This designation includes any isomers and hydrates, as well as any solutions and mixtures containing this substance.
[40 CFR 116.4 (7/1/99)] **QC REVIEWED**

For the protection of human health from the toxic properties of ethylbenzene ... the ambient water criterion is determined to be 1.4 mg/l.
[USEPA; Quality Criteria for Water 1986: Ethylbenzene (May 1,1986) EPA 440/5-86-001] **QC REVIEWED**

The maximum contaminant level (MCL) set forth by the National Revised Primary Drinking Water Regulations for the organic contaminant ethylbenzene in community and non-transient, non-community water systems is 0.7 mg/l.
[40 CFR 141.61 (7/1/99)] **QC REVIEWED**

Federal Drinking Water Standards:

EPA 700 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

Federal Drinking Water Guidelines:

EPA 700 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

State Drinking Water Guidelines:

(AZ) ARIZONA 680 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

(FL) FLORIDA 30 ug/l

[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

(ME) MAINE 700 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

(MN) MINNESOTA 700 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Acceptable Daily Intakes:

Acceptable daily intake: 1.6 mg/day

[USEPA; Ambient Water Quality Criteria Doc: Ethylbenzene p.C-22 (1980) EPA 440/5-80-048]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

TSCA Requirements:

Pursuant to section 8(d) of TSCA, EPA promulgated a model Health and Safety Data Reporting Rule. The section 8(d) model rule requires manufacturers, importers, and processors of listed chemical substances and mixtures to submit to EPA copies and lists of unpublished health and safety studies. Ethylbenzene is included on this list.

[40 CFR 716.120 (7/1/99)]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

CERCLA Reportable Quantities:

Persons in charge of vessels or facilities are required to notify the National Response Center (NRC) immediately, when there is a release of this designated hazardous substance, in an amount equal to or greater than its reportable quantity of 1000 lb or 454 kg. The toll free number of the NRC is (800) 424-8802; In the Washington D.C. metropolitan area (202) 426-2675. The rule for determining when notification is required is stated in 40 CFR 302.4 (section IV. D.3.b).
[40 CFR 302.4 (7/1/99)]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

RCRA Requirements:

F003; When ethylbenzene is a spent solvent, it is classified as a hazardous waste from a nonspecific source (F003), as stated in 40 CFR 261.31, and must be managed according to State and/or Federal hazardous waste regulations.

[40 CFR 261.31 (7/1/99)]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Atmospheric Standards:

This action promulgates standards of performance for equipment leaks of Volatile Organic Compounds (VOC) in the Synthetic Organic Chemical Manufacturing Industry (SOCMI). The intended effect of these standards is to require all newly constructed, modified, and reconstructed SOCMI process units to use the best demonstrated system of continuous emission reduction for equipment leaks of VOC, considering costs, non air quality health and environmental impact and energy requirements. Ethylbenzene is produced, as an intermediate or a final product, by process units covered under this subpart.

[40 CFR 60.489 (7/1/99)]**PEER REVIEWED**

Listed as a hazardous air pollutant (HAP) generally known or suspected to cause serious health problems. The Clean Air Act, as amended in 1990, directs EPA to set standards requiring major sources to sharply reduce routine emissions of toxic pollutants. EPA is required to establish and phase in specific performance based standards for all air emission sources that emit one or more of the listed pollutants. Ethylbenzene is included on this list.

[Clean Air Act as amended in 1990, Sect. 112 (b) (1) Public Law 101-549 Nov. 15, 1990]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Clean Water Act Requirements:

Toxic pollutant designated pursuant to section 307(a)(1) of the Federal Water Pollution Control Act and is subject to effluent limitations.
[40 CFR 401.15 (7/1/99)] **QC REVIEWED**

Ethylbenzene is designated as a hazardous substance under section 311(b)(2)(A) of the Federal Water Pollution Control Act and further regulated by the Clean Water Act Amendments of 1977 and 1978. These regulations apply to discharges of this substance. This designation includes any isomers and hydrates, as well as any solutions and mixtures containing this substance.
[40 CFR 116.4 (7/1/99)] **QC REVIEWED**

For the protection of human health from the toxic properties of ethylbenzene ... the ambient water criterion is determined to be 1.4 mg/l.
[USEPA; Quality Criteria for Water 1986: Ethylbenzene (May 1,1986) EPA 440/5-86-001] **QC REVIEWED**

The maximum contaminant level (MCL) set forth by the National Revised Primary Drinking Water Regulations for the organic contaminant ethylbenzene in community and non-transient, non-community water systems is 0.7 mg/l.
[40 CFR 141.61 (7/1/99)] **QC REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Federal Drinking Water Standards:

EPA 700 ug/l

[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Federal Drinking Water Guidelines:

EPA 700 ug/l

[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

State Drinking Water Guidelines:

(AZ) ARIZONA 680 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

(FL) FLORIDA 30 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

(ME) MAINE 700 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

(MN) MINNESOTA 700 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Chemical/Physical Properties:

Molecular Formula:

C8-H10
PEER REVIEWED

Molecular Weight:

106.16
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 643]**PEER REVIEWED**

Color/Form:

Colorless liquid
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 1997. 461]**PEER REVIEWED**

Odor:

Aromatic odor
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 1997. 461]**PEER REVIEWED**

Pungent odor
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1342]**PEER REVIEWED**

SWEET, GASOLINE-LIKE ODOR
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Boiling Point:

136.1 deg C
[Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 79th ed. Boca Raton, FL: CRC Press Inc., 1998-1999.,p. 3-47]**PEER REVIEWED**

Melting Point:

-94.9 deg C
[Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 79th ed.

Boca Raton, FL: CRC Press Inc., 1998-1999.,p. 3-47]**PEER REVIEWED**

Critical Temperature & Pressure:

Critical temperature = 617.15 K; critical pressure = 3.6X10+6 Pa
[Daubert, T.E., R.P. Danner. Physical and Thermodynamic Properties of Pure Chemicals Data Compilation. Washington, D.C.: Taylor and Francis, 1989.]**PEER REVIEWED**

Density/Specific Gravity:

0.8670 @ 20 deg C/4 deg C
[Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 79th ed. Boca Raton, FL: CRC Press Inc., 1998-1999.,p. 3-47]**PEER REVIEWED**

Heat of Combustion:

-17,780 BTU/lb= -9877 cal/g= -413.5x10+5 J/kg
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Heat of Vaporization:

4.8X10+7 J/kmol @ 178.20 K
[Daubert, T.E., R.P. Danner. Physical and Thermodynamic Properties of Pure Chemicals Data Compilation. Washington, D.C.: Taylor and Francis, 1989.]**PEER REVIEWED**

Octanol/Water Partition Coefficient:

log Kow= 3.15
[Hansch, C., Leo, A., D. Hoekman. Exploring QSAR - Hydrophobic, Electronic, and Steric Constants. Washington, DC: American Chemical Society., 1995. 43]**PEER REVIEWED**

Solubilities:

SOL IN ALL PROPORTIONS IN ETHYL ALCOHOL AND ETHYL ETHER
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 2114]**PEER REVIEWED**

SOLUBILITY IN WATER @ 15 DEG C, 0.014 G/100 ML
[Patty, F. (ed.). Industrial Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New York: Interscience Publishers, 1963. 1223]**PEER REVIEWED**

Miscible with the usual organic solvents.
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc.,

1996. 643]**PEER REVIEWED**

Soluble in alcohol, benzene, carbon tetrachloride, and ether.
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 1997. 461]**PEER REVIEWED**

Slight soluble in chloroform; miscible in ethanol and ethyl ether.
[Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 79th ed. Boca Raton, FL: CRC Press Inc., 1998-1999.,p. 3-47]**PEER REVIEWED**

In water, 169 mg/l @ 25 deg C
[Sanemasa I et al; Bull Chem Soc Japan 55: 1054-62 (1982)]**PEER REVIEWED**

Insol in ammonia; sol in SO2.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1522]**PEER REVIEWED**

Spectral Properties:

SADTLER REF NUMBER: 246 (IR, PRISM); 82 (IR, GRATING)
[Weast, R.C. (ed.). Handbook of Chemistry and Physics. 60th ed. Boca Raton, Florida: CRC Press Inc., 1979.,p. C-165]**PEER REVIEWED**

IR: 4779 (Coblentz Society Spectral Collection)
[Weast, R.C. and M.J. Astle. CRC Handbook of Data on Organic Compounds. Volumes I and II. Boca Raton, FL: CRC Press Inc. 1985.,p. V1 613]**PEER REVIEWED**

UV: 97 (Sadtler Research Laboratories Spectral Collection)
[Weast, R.C. and M.J. Astle. CRC Handbook of Data on Organic Compounds. Volumes I and II. Boca Raton, FL: CRC Press Inc. 1985.,p. V1 613]**PEER REVIEWED**

NMR: 505 (Varian Associates NMR Spectra Catalogue)
[Weast, R.C. and M.J. Astle. CRC Handbook of Data on Organic Compounds. Volumes I and II. Boca Raton, FL: CRC Press Inc. 1985.,p. V1 613]**PEER REVIEWED**

MASS: 322 (Atlas of Mass Spectral Data, John Wiley & Sons, New York)
[Weast, R.C. and M.J. Astle. CRC Handbook of Data on Organic Compounds. Volumes I and II. Boca Raton, FL: CRC Press Inc. 1985.,p. V1 613]**PEER REVIEWED**

Index of refraction: 1.4959 at 20 deg C/D
[Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 79th ed. Boca Raton, FL: CRC Press Inc., 1998-1999.,p. 3-47]**PEER REVIEWED**

Surface Tension:

4.3 N/m @ 178.20 K
[Daubert, T.E., R.P. Danner. Physical and Thermodynamic Properties of Pure Chemicals Data Compilation. Washington, D.C.: Taylor and Francis, 1989.]**PEER REVIEWED**

Vapor Density:

3.66 (Air= 1)
[Sax, N.I. Dangerous Properties of Industrial Materials. Vol 1-3 7th ed. New York, NY: Van Nostrand Reinhold, 1989. 1601]**PEER REVIEWED**

Vapor Pressure:

9.6 mm Hg @ 25 deg C
[Daubert, T.E., R.P. Danner. Physical and Thermodynamic Properties of Pure Chemicals Data Compilation. Washington, D.C.: Taylor and Francis, 1989.]**PEER REVIEWED**

Relative Evaporation Rate:

IT EVAPORATES ABOUT 94 TIMES MORE SLOWLY THAN ETHER
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1342]**PEER REVIEWED**

Viscosity:

0.64 cP @ 25 deg C
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 1997. 461]**PEER REVIEWED**

Other Chemical/Physical Properties:

DENSITY OF SATURATED VAPOR-AIR MIXTURE AT 760 MM HG (AIR= 1): 1.03 (26 DEG C); SPECIFIC DISPERSION: 174.6
[Patty, F. (ed.). Industrial Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New York: Interscience Publishers, 1963. 1223]**PEER REVIEWED**

CONVERSION FACTORS: 1 MG/L IS EQUIVALENT TO 230 PPM, 1 PPM IS EQUIVALENT TO 4.35 MG/CU M AT 25 DEG C, 760 MM HG
[Patty, F. (ed.). Industrial Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New York: Interscience Publishers, 1963. 1231]**PEER REVIEWED**

Specific heat: 0.41 cal/gal/K
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 1997. 461]**PEER REVIEWED**

Liquid-water interfacial tension: 35.48 dynes/cm= 0.03548 N/m @ 20 deg C

[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Ratio of Specific Heats of Vapor (gas): 1.071
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Heats of transition, J/(mol.K): fusion 9.164; formation @ 25 deg C: -12.456; entropy of formation 255.2
[Kirk-Othmer Encyclopedia of Chemical Technology. 4th ed. Volumes 1: New York, NY. John Wiley and Sons, 1991-Present.,p. V5 833]**PEER REVIEWED**

Cricital density: 2.67 mmol/cu m; critical volume: 374.0 cu m/mol
[Kirk-Othmer Encyclopedia of Chemical Technology. 4th ed. Volumes 1: New York, NY. John Wiley and Sons, 1991-Present.,p. V25 833]**PEER REVIEWED**

Viscosity: 0.678 mPas (20 deg C)
[Environment Canada; Tech Info for Problem Spills: Ethylbenzene p.4 (1981)]**PEER REVIEWED**

Ionization potential: 8.76 eV
[Environment Canada; Tech Info for Problem Spills: Ethylbenzene p.4 (1981)]**PEER REVIEWED**

Flame speed: 0.35 m/s
[Environment Canada; Tech Info for Problem Spills: Ethylbenzene p.2 (1981)]**PEER REVIEWED**

Partition coefficients at 37 deg C for ethylbenzene into blood= 28.4; into oil= 3,790.
[Sato A, Nakajima T; Scand J Work Environ Health 13: 81-93 (1987)]**PEER REVIEWED**

Henry's Law constant= 7.88X10-3 atm-cu m/mol @ 25 deg C
[Sanemasa I et al; Bull Chem Soc Japan 55: 1054-62 (1982)]**PEER REVIEWED**

Hydroxyl radical rate constant= 7.10X10-12 cu m/molecule-sec @ 25 deg C
[Atkinson R; J Phys Chem Ref Data Monograph No. 2 p. 48 (1994)]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Molecular Formula:

C8-H10

PEER REVIEWED

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Molecular Weight:

106.16

[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 643]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Color/Form:

Colorless liquid

[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 1997. 461]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Odor:

Aromatic odor

[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 1997. 461]**PEER REVIEWED**

Pungent odor

[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1342]**PEER REVIEWED**

SWEET, GASOLINE-LIKE ODOR

[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Boiling Point:

136.1 deg C

[Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 79th ed. Boca Raton, FL: CRC Press Inc., 1998-1999.,p. 3-47]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Melting Point:

-94.9 deg C

[Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 79th ed. Boca Raton, FL: CRC Press Inc., 1998-1999.,p. 3-47]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Critical Temperature & Pressure:

Critical temperature = 617.15 K; critical pressure = 3.6X10+6 Pa

[Daubert, T.E., R.P. Danner. Physical and Thermodynamic Properties of Pure Chemicals Data Compilation. Washington, D.C.: Taylor and Francis, 1989.]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Density/Specific Gravity:

0.8670 @ 20 deg C/4 deg C

[Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 79th ed. Boca Raton, FL: CRC Press Inc., 1998-1999.,p. 3-47]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Heat of Combustion:

-17,780 BTU/lb= -9877 cal/g= -413.5x10+5 J/kg

[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Heat of Vaporization:

4.8X10+7 J/kmol @ 178.20 K

[Daubert, T.E., R.P. Danner. Physical and Thermodynamic Properties of Pure Chemicals Data Compilation. Washington, D.C.: Taylor and Francis, 1989.]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Octanol/Water Partition Coefficient:

log Kow= 3.15

[Hansch, C., Leo, A., D. Hoekman. Exploring QSAR - Hydrophobic, Electronic, and Steric Constants. Washington, DC: American Chemical Society., 1995. 43]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Solubilities:

SOL IN ALL PROPORTIONS IN ETHYL ALCOHOL AND ETHYL ETHER
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 2114]**PEER REVIEWED**

SOLUBILITY IN WATER @ 15 DEG C, 0.014 G/100 ML
[Patty, F. (ed.). Industrial Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New York: Interscience Publishers, 1963. 1223]**PEER REVIEWED**

Miscible with the usual organic solvents.
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 643]**PEER REVIEWED**

Soluble in alcohol, benzene, carbon tetrachloride, and ether.
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 1997. 461]**PEER REVIEWED**

Slight soluble in chloroform; miscible in ethanol and ethyl ether.
[Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 79th ed. Boca Raton, FL: CRC Press Inc., 1998-1999.,p. 3-47]**PEER REVIEWED**

In water, 169 mg/l @ 25 deg C
[Sanemasa I et al; Bull Chem Soc Japan 55: 1054-62 (1982)]**PEER REVIEWED**

Insol in ammonia; sol in SO2.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1522]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Spectral Properties:

SADTLER REF NUMBER: 246 (IR, PRISM); 82 (IR, GRATING)

[Weast, R.C. (ed.). Handbook of Chemistry and Physics. 60th ed. Boca Raton, Florida: CRC Press Inc., 1979.,p. C-165]**PEER REVIEWED**

IR: 4779 (Coblentz Society Spectral Collection)

[Weast, R.C. and M.J. Astle. CRC Handbook of Data on Organic Compounds. Volumes I and II. Boca Raton, FL: CRC Press Inc. 1985.,p. V1 613]**PEER REVIEWED**

UV: 97 (Sadtler Research Laboratories Spectral Collection)

[Weast, R.C. and M.J. Astle. CRC Handbook of Data on Organic Compounds. Volumes I and II. Boca Raton, FL: CRC Press Inc. 1985.,p. V1 613]**PEER REVIEWED**

NMR: 505 (Varian Associates NMR Spectra Catalogue)

[Weast, R.C. and M.J. Astle. CRC Handbook of Data on Organic Compounds. Volumes I and II. Boca Raton, FL: CRC Press Inc. 1985.,p. V1 613]**PEER REVIEWED**

MASS: 322 (Atlas of Mass Spectral Data, John Wiley & Sons, New York)

[Weast, R.C. and M.J. Astle. CRC Handbook of Data on Organic Compounds. Volumes I and II. Boca Raton, FL: CRC Press Inc. 1985.,p. V1 613]**PEER REVIEWED**

Index of refraction: 1.4959 at 20 deg C/D

[Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 79th ed. Boca Raton, FL: CRC Press Inc., 1998-1999.,p. 3-47]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Surface Tension:

4.3 N/m @ 178.20 K

[Daubert, T.E., R.P. Danner. Physical and Thermodynamic Properties of Pure Chemicals Data Compilation. Washington, D.C.: Taylor and Francis, 1989.]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Vapor Density:

3.66 (Air= 1)

[Sax, N.I. Dangerous Properties of Industrial Materials. Vol 1-3 7th ed. New York, NY: Van Nostrand Reinhold, 1989. 1601]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Vapor Pressure:

9.6 mm Hg @ 25 deg C

[Daubert, T.E., R.P. Danner. Physical and Thermodynamic Properties of Pure Chemicals Data Compilation. Washington, D.C.: Taylor and Francis, 1989.]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Relative Evaporation Rate:

IT EVAPORATES ABOUT 94 TIMES MORE SLOWLY THAN ETHER
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1342]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Viscosity:

0.64 cP @ 25 deg C

[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 1997. 461]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Other Chemical/Physical Properties:

DENSITY OF SATURATED VAPOR-AIR MIXTURE AT 760 MM HG (AIR= 1): 1.03 (26 DEG C); SPECIFIC DISPERSION: 174.6

[Patty, F. (ed.). Industrial Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New York: Interscience Publishers, 1963. 1223]**PEER REVIEWED**

CONVERSION FACTORS: 1 MG/L IS EQUIVALENT TO 230 PPM, 1 PPM IS EQUIVALENT TO 4.35 MG/CU M AT 25 DEG C, 760 MM HG

[Patty, F. (ed.). Industrial Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New York: Interscience Publishers, 1963. 1231]**PEER REVIEWED**

Specific heat: 0.41 cal/gal/K

[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 1997. 461]**PEER REVIEWED**

Liquid-water interfacial tension: 35.48 dynes/cm= 0.03548 N/m @ 20 deg C

[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Ratio of Specific Heats of Vapor (gas): 1.071

[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Heats of transition, J/(mol.K): fusion 9.164; formation @ 25 deg C: -12.456; entropy of formation 255.2

[Kirk-Othmer Encyclopedia of Chemical Technology. 4th ed. Volumes 1: New York, NY. John Wiley and Sons, 1991-Present.,p. V5 833]**PEER REVIEWED**

Cricital density: 2.67 mmol/cu m; critical volume: 374.0 cu m/mol

[Kirk-Othmer Encyclopedia of Chemical Technology. 4th ed. Volumes 1: New York, NY. John Wiley and Sons, 1991-Present.,p. V25 833]**PEER REVIEWED**

Viscosity: 0.678 mPas (20 deg C)

[Environment Canada; Tech Info for Problem Spills: Ethylbenzene p.4 (1981)]**PEER REVIEWED**

Ionization potential: 8.76 eV

[Environment Canada; Tech Info for Problem Spills: Ethylbenzene p.4 (1981)]**PEER REVIEWED**

Flame speed: 0.35 m/s
[Environment Canada; Tech Info for Problem Spills: Ethylbenzene p.2 (1981)]**PEER REVIEWED**

Partition coefficients at 37 deg C for ethylbenzene into blood= 28.4; into oil= 3,790.
[Sato A, Nakajima T; Scand J Work Environ Health 13: 81-93 (1987)]**PEER REVIEWED**

Henry's Law constant= 7.88X10-3 atm-cu m/mol @ 25 deg C
[Sanemasa I et al; Bull Chem Soc Japan 55: 1054-62 (1982)]**PEER REVIEWED**

Hydroxyl radical rate constant= 7.10X10-12 cu m/molecule-sec @ 25 deg C
[Atkinson R; J Phys Chem Ref Data Monograph No. 2 p. 48 (1994)]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Chemical Safety & Handling:

DOT Emergency Guidelines:

Fire or explosion: Highly flammable: Will be easily ignited by heat, sparks or flames. Vapors may form explosive mixtures with air. Vapors may travel to source of ignition and flash back. Most vapors are heavier than air. They will spread along ground and collect in low confined areas (sewers, basements, tanks). Vapor explosion hazard indoors, outdoors or in sewers. Some may polymerize (P) explosively when heated or involved in a fire. Runoff to sewer may create fire or explosion hazard. Containers may explode when heated. Many liquids are lighter than water.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

Health: May cause toxic effects if inhaled or absorbed through skin. Inhalation or contact with material may irritate or burn skin and eyes. Fire will produce irritating, corrosive and/or toxic gases. Vapors may cause dizziness or suffocation. Runoff from fire control or dilution water may cause pollution.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

Public safety: Call Emergency Response Telephone Number. ... Isolate spill or leak area immediately for at least 50 to lOO meters (160 to 330 feet) in all directions. Keep unauthorized personnel away. Stay upwind. Keep out of low areas. Ventilate closed spaces before entering.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

Protective clothing: Wear positive pressure self-contained breathing apparatus (SCBA). Structural firefighters' protective clothing will only provide limited protection.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs

Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

Evacuation: Large spill: Consider initial downwind evacuation for at least 300 meters (1000 feet). Fire: If tank, rail car or tank truck is involved in a fire, isolate for 800 meters (1/2 mile) in all directions; also, consider initial evacuation for 800 meters (1/2 mile) in all directions.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

Fire: Caution: All these products have a very low flash point: Use of water spray when fighting fire may be inefficient. Small fires: Dry chemical, CO2, water spray or alcohol-resistant foam. Do not use dry chemical extinguishers to control fires involving nitromethane or nitroethane. Large fires: Water spray, fog or alcohol-resistant foam. Do not use straight streams. Move containers from fire area if you can do it without risk. Fire involving tanks or car/trailer loads: Fight fire from maximum distance or use unmanned hose holders or monitor nozzles. Cool containers with flooding quantities of water until well after fire is out. Withdraw immediately in case of rising sound from venting safety devices or discoloration of tank. Always stay away from the ends of tanks. For massive fire, use unmanned hose holders or monitor nozzles; if this is impossible, withdraw from area and let fire burn.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

Spill or leak: Eliminate all ignition sources (no smoking, flares, sparks or flames in immediate area). All equipment used when handling the product must be grounded. Do not touch or walk through spilled material. Stop leak if you can do it without risk. Prevent entry into waterways, sewers, basements or confined areas. A vapor suppressing foam may be used to reduce vapors. Absorb or cover with dry earth, sand or other non-combustible material and transfer to containers. Use clean non-sparking tools to collect absorbed material. Large spills: Dike far ahead of liquid spill for later disposal. Water spray may reduce vapor; but may not prevent ignition in closed spaces.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

First aid: Move victim to fresh air. Call emergency medical care. Apply artificial respiration if victim is not breathing. Administer oxygen if breathing is difficult. Remove and isolate contaminated clothing and shoes. In case of contact with substance, immediately flush skin or eyes with running water for at least 20 minutes. Wash skin with soap and water. Keep victim warm and quiet. Effects of exposure (inhalation,

ingestion or skin contact) to substance may be delayed. Ensure that medical personnel are aware of the material(s) involved, and take precautions to protect themselves.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

Odor Threshold:

140 ppm /Purity not specified/
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

2-2.6 mg/cu m; detection: 0.4 mg/cu m /Purity not specified/
[Verschueren, K. Handbook of Environmental Data on Organic Chemicals. 3rd ed. New York, NY: Van Nostrand Reinhold Co., 1996. 944]**PEER REVIEWED**

Odor Low: 8.7 mg/cu m, Odor High: 870.0 mg/cu m
[Ruth JH; Am Ind Hyg Assoc J 47: A-142-51 (1986)]**PEER REVIEWED**

Skin, Eye and Respiratory Irritations:

... CHARACTERIZED ... AS MOST SEVERE IRRITANT OF THE BENZENE SERIES.
[American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices. 5th ed. Cincinnati, OH:American Conference of Governmental Industrial Hygienists, 1986. 244]**PEER REVIEWED**

A concn of 200 ppm causes eye irritation. A concn of 100 ppm for 8 hr caused irritative effects in a human.
[Cleland, J.G., G.L. Kingsbury. Multimedia Environmental Goals for Environmental Assessment. Volume 1. EPA-600/7-77-136a. Research Triangle Park, NC: EPA, Nov. 1977.,p. E-148]**PEER REVIEWED**

EXPOSURE TO CONCN OF 5000 PPM /24.6 MG/L/ ... CAUSES INTOLERABLE IRRITATION OF EYES, MUCOUS MEMBRANES & NOSE.
[Patty, F. (ed.). Industrial Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New York: Interscience Publishers, 1963. 1232]**PEER REVIEWED**

HAZARD WARNING: ... exposure to 21.5 g/cu m (5000 ppm) ethylbenzene for a few seconds gives intolerable irritation of nose, eyes, and throat.
[Environmental Health Criteria 186: Ethylbenzene pp. 67 (1996) by the International Programme on Chemical Safety (IPCS) under the joint sponsorship of the United Nations Environment Programme, the

International Labour Organisation and the World Health Organization.]**QC REVIEWED**

Fire Potential:

A very dangerous fire ... hazard when exposed to heat or flame ...
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1522]**PEER REVIEWED**

Electrical ignition hazard: May be ignited by static discharge.
[Environment Canada; Tech Info for Problem Spills: Ethylbenzene (Draft) p.4 (1982)]**PEER REVIEWED**

NFPA Hazard Classification:

Health: 2. 2= Materials that, on intense or continued (but not chronic) exposure, could cause temporary incapacitation or possible residual injury, including those requiring the use of respiratory protective equipment that has an independent air supply. These materials are hazardous to health, but areas may be entered freely if personnel are provided with full-face mask self-contained breathing apparatus that provides complete eye protection.
[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 325-48]**PEER REVIEWED**

Flammability: 3. 3= This degree includes Class IB and IC flammable liquids and materials that can be easily ignited under almost all normal temperature conditions. Water may be ineffective in controlling or extinguishing fires in such materials.
[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 325-48]**PEER REVIEWED**

Reactivity: 0. 0= This degree includes materials that are normally stable, even under fire exposure conditions, and that do not react with water. Normal fire fighting procedures may be used.
[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 325-48]**PEER REVIEWED**

Flammable Limits:

Lower flammable limit: 0.8% by volume; Upper flammable limit: 6.7% by volume
[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 325-48]**PEER REVIEWED**

Flash Point:

12.8 DEG C (55 DEG F) (CLOSED CUP)
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New

York, NY: John Wiley & Sons Inc., 1993-1994. 1304]**PEER REVIEWED**

Autoignition Temperature:

810 DEG F
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1522]**PEER REVIEWED**

Fire Fighting Procedures:

Approach fire from upwind to avoid hazardous vapors and toxic decomposition products. Use water spray, dry chemical, foam, or carbon dioxide. Use water spray to keep fire-exposed containers cool.
[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 49-65]**PEER REVIEWED**

If material on fire or involved in fire: Do not extinguish fire unless flow can be stopped or safely confined. Use water in flooding quantities as fog. Solid streams of water may spread fire. Cool all affected containers with flooding quantities of water. Apply water from as far a distance as possible. Use foam, carbon dioxide, or dry chemical.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 443]**PEER REVIEWED**

Toxic Combustion Products:

Irritating vapors are generated when heated.
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

The combustion products of ethylbenzene are water and carbon dioxide or carbon monoxide in limited oxygen atmospheres.
[Environment Canada; Tech Info for Problem Spills: Ethylbenzene (Draft) p.79 (1982)]**PEER REVIEWED**

Compounds identified in tars produced by the pyrolysis of ethylbenzene include the following suspected carcinogens: 1-benzanthracene, benzene, benzofluoranthene, 10,11-benzofluoranthene, 12-benzofluoranthene, 1-benzofluoranthene, 1-benzopyrene, 3,4-benzopyrene, chrysene, and 1,2:5,6-dibenzanthracene.
[NAS; The Alkylbenzenes p.99 (1981)]**PEER REVIEWED**

Firefighting Hazards:

Vapors are heavier than air and may travel to a source of ignition and flash back. Liquid floats on water and may travel to a source of ignition and spread fire.
[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 49-65]**PEER REVIEWED**

Explosive Limits & Potential:

Vapors form explosive mixtures with air.
[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 49-65]**PEER REVIEWED**

Lower explosive limit= 1.2%. Upper explosive limit= 6.8%.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1522]**PEER REVIEWED**

Hazardous Reactivities & Incompatibilities:

Incompatibilities: Strong oxidizers.
[Sittig, M. Handbook of Toxic and Hazardous Chemicals and Carcinogens, 1985. 2nd ed. Park Ridge, NJ: Noyes Data Corporation, 1985. 4122]**PEER REVIEWED**

... Can react vigorously with oxidizing materials.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1522]**PEER REVIEWED**

Strong oxidizers.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 132]**PEER REVIEWED**

Hazardous Decomposition:

When heated to decomposition it emits acrid smoke and irritating fumes.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1522]**PEER REVIEWED**

Immediately Dangerous to Life or Health:

800 ppm
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 132]**PEER REVIEWED**

Protective Equipment & Clothing:

Wear full protective clothing and positive pressure self-contained breathing apparatus.
[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 49-65]**PEER REVIEWED**

Rubber overclothing (including gloves)
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Wear appropriate personal protective clothing to prevent skin contact.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 132]**PEER REVIEWED**

Wear appropriate eye protection to prevent eye contact.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 132]**PEER REVIEWED**

Recommendations for respirator selection. Max concn for use: 800 ppm. Respirator Class(es): Any chemical cartridge respirator with organic vapor cartridge(s). May require eye protection. Any air-purifying, full-facepiece respirator (gas mask) with a chin-style, front- or back-mounted organic vapor canister. Any powered, air-purifying respirator with organic vapor cartridge(s). May require eye protection. Any supplied-air respirator. May require eye protection. Any self-contained breathing apparatus with a full facepiece.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 132]**PEER REVIEWED**

Recommendations for respirator selection. Condition: Emergency or planned entry into unknown concn or IDLH conditions: Respirator Class(es): Any self-contained breathing apparatus that has a full facepiece and is operated in a pressure-demand or other positive-pressure mode. Any supplied-air respirator that has a full facepiece and is operated in a pressure-demand or other positive-pressure mode in combination with an auxiliary self-contained breathing apparatus operated in pressure-demand or other positive-pressure mode.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 132]**PEER REVIEWED**

Recommendations for respirator selection. Condition: Escape from suddenly occurring respiratory hazards: Respirator Class(es): Any air-purifying, full-facepiece respirator (gas mask) with a chin-style, front- or back-mounted organic vapor canister. Any appropriate escape-type, self-contained breathing apparatus.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 132]**PEER REVIEWED**

Preventive Measures:

Contact lenses should not be worn when working with this chemical.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 132]**PEER REVIEWED**

SRP: The scientific literature for the use of contact lenses in industry is conflicting. The benefit or detrimental effects of wearing contact lenses depend not only upon the substance, but also on factors including the form of the substance, characteristics and duration of the exposure, the uses of other eye

protection equipment, and the hygiene of the lenses. However, there may be individual substances whose irritating or corrosive properties are such that the wearing of contact lenses would be harmful to the eye. In those specific cases, contact lenses should not be worn. In any event, the usual eye protection equipment should be worn even when contact lenses are in place.
PEER REVIEWED

Employees should wash promptly when skin is wet or contaminated. Remove clothing immediately if wet or contaminated to avoid flammability hazard.
[Sittig, M. Handbook of Toxic and Hazardous Chemicals and Carcinogens, 1985. 2nd ed. Park Ridge, NJ: Noyes Data Corporation, 1985. 414]**PEER REVIEWED**

BEFORE WORKERS ARE ALLOWED TO ENTER A REACTION VESSEL ... THE VESSEL SHOULD BE PURGED AND WELL VENTILATED. PERSONAL PROTECTIVE EQUIPMENT SHOULD BE SUPPLIED ...
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 2114]**PEER REVIEWED**

... SUBSTITUTION OF LESS IRRITATING SUBSTANCES, ... REDESIGN OF OPERATIONS, ... PREVENT CONTACT, PROVISION OF A PHYSICAL BARRIER AGAINST CONTACT, PROPER WASHING FACILITIES, PROPER WORK CLOTHING AND STORAGE FACILITIES, PROTECTIVE CLOTHING, BARRIER CREAMS, AND MEDICAL CONTROL ...
[Sax, N.I. Dangerous Properties of Industrial Materials. 4th ed. New York: Van Nostrand Reinhold, 1975. 727]**PEER REVIEWED**

Personnel protection: Avoid breathing vapors. Keep upwind. ... Do not handle broken packages without protective equipment. Wash away any material which may have contacted the body with copious amounts of water or soap and water.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 443]**PEER REVIEWED**

COMBUSTION MAY BE IMPROVED BY MIXING WITH MORE FLAMMABLE LIQ. ... SHOULD NOT BE ALLOWED TO ENTER CONFINED SPACE, SUCH AS SEWER, BECAUSE OF POSSIBILITY OF EXPLOSION.
[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) PublicationNo. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981. 2]**PEER REVIEWED**

If material not on fire and not involved in fire: Keep sparks, flames, and other sources of ignition away. Keep material out of water sources and sewers. Build dikes to contain flow as necessary. Attempt to stop leak if without hazard. Use water spray to knock-down vapors.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 443]**PEER REVIEWED**

The worker should immediately wash the skin when it becomes contaminated.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 132]**PEER REVIEWED**

Work clothing that becomes wet should be immediately removed due to its flammability hazard.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 132]**PEER REVIEWED**

Shipment Methods and Regulations:

No person may /transport,/ offer or accept a hazardous material for transportation in commerce unless that person is registered in conformance ... and the hazardous material is properly classed, described, packaged, marked, labeled, and in condition for shipment as required or authorized by ... /the hazardous materials regulations (49 CFR 171-177)./
[49 CFR 171.2 (7/1/99)]**PEER REVIEWED**

The International Air Transport Association (IATA) Dangerous Goods Regulations are published by the IATA Dangerous Goods Board pursuant to IATA Resolutions 618 and 619 and constitute a manual of industry carrier regulations to be followed by all IATA Member airlines when transporting hazardous materials.
[IATA. Dangerous Goods Regulations. 40th Ed. Montreal, Canada and Geneva, Switzerland: International Air Transport Association, Dangerous Goods Regulations, 1999. 149]**PEER REVIEWED**

The International Maritime Dangerous Goods Code lays down basic principles for transporting hazardous chemicals. Detailed recommendations for individual substances and a number of recommendations for good practice are included in the classes dealing with such substances. A general index of technical names has also been compiled. This index should always be consulted when attempting to locate the appropriate procedures to be used when shipping any substance or article.
[IMDG; International Maritime Dangerous Goods Code; International Maritime Organization p.3222 (1998)]**PEER REVIEWED**

Storage Conditions:

Outside or detached storage is preferred. Inside storage should be in a standard flammable liquids storage warehouse, room, or cabinet. Separate from oxidizing materials.
[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 49-65]**PEER REVIEWED**

Temp: ambient; Venting: open (flame arrester) or pressure-vacuum
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Cleanup Methods:

1) REMOVE ALL IGNITION SOURCES. 2) VENTILATE AREA OF SPILL OR LEAK. 3) FOR

SMALL QUANTITIES, ABSORB ON PAPER TOWELS. EVAPORATE IN SAFE PLACE (SUCH AS FUME HOOD). ... BURN PAPER IN SUITABLE LOCATION AWAY FROM COMBUSTIBLE MATERIALS. LARGE QUANTITIES CAN BE COLLECTED & ATOMIZED IN SUITABLE COMBUSTION CHAMBER.
[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) PublicationNo. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981. 1]**PEER REVIEWED**

Land spills should be contained; skimming equipment and/or sorbent (polyurethane) foams can be used. Use of activated carbon is recommended.
[Environment Canada; Tech Info for Problem Spills: Ethylbenzene p.83 (1982)]**PEER REVIEWED**

Water spills should be contained; skimming equipment and/or sorbent (polyurethane) foams can be used to remove the slick. Universal gelling agent can be used to solidify a trapped mass. Use of activated carbon on dissolved portion is recommended.
[Environment Canada; Tech Info for Problem Spills: Ethylbenzene p.83 (1982)]**PEER REVIEWED**

Environmental considerations: Land spill: Dig a pit, pond, lagoon, or holding area to contain liquid or solid material. /SRP: If time permits, pits, ponds, lagoons, soak holes, or holding areas should be sealed with an impermeable flexible membrane liner./ Dike surface flow using sand bags, foamed polyurethane, or foamed concrete. Absorb bulk liquid with fly ash, cement powder, sawdust, or commercial sorbents. Apply "universal" gelling agent to immobilize spill. Apply appropriate foam to diminish vapor and fire hazard.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 443]**PEER REVIEWED**

Environmental considerations - Air spill: Apply water spray or mist to knock down vapors.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 443]**PEER REVIEWED**

Environmental considerations: Water spill: Use natural barriers or oil spill control booms to limit spill travel. Use surface active agent (e.g., detergent, soaps, alcohols), if approved by EPA. Inject "universal" gelling agent to solidify encircled spill and increase effectiveness of booms. If dissolved, in region of 10 ppm or greater concentration, apply activated carbon at ten times the spilled amount. Remove trapped material with suction hoses. Use mechanical dredges or lifts to remove immobilized masses of pollutants and precipitates.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 443]**PEER REVIEWED**

ABSORB IN VERMICULITE, DRY SAND, EARTH OR SIMILAR MATERIAL
[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards.

DHHS(NIOSH) PublicationNo. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981. 2]**PEER REVIEWED**

Disposal Methods:

Generators of waste (equal to or greater than 100 kg/mo) containing this contaminant, EPA hazardous waste number F003, must conform with USEPA regulations in storage, transportation, treatment and disposal of waste.
[40 CFR 240-280, 300-306, 702-799 (7/1/90)]**PEER REVIEWED**

Ethylbenzene is a waste chemical stream constituent which may be subjected to ultimate disposal by controlled incineration.
[USEPA; Engineering Handbook for Hazardous Waste Incineration p.2-6 (1981) EPA 68-03-3025]**PEER REVIEWED**

A good candidate for liquid injection incineration at a temperature range of 650 to 1,600 deg C and a residence time of 0.1 to 2 seconds. A good candidate for rotary kiln incineration at a temperature range of 820 to 1,600 deg C and residence times of seconds for liquids and gases, and hours for solids. A good candidate for fluidized bed incineration at a temperature range of 450 to 980 deg C and residence times of seconds for liquids and gases, and longer for solids.
[USEPA; Engineering Handbook for Hazardous Waste Incineration p.3-4 (1981) EPA 68-03-3025]**PEER REVIEWED**

The following wastewater treatment technologies have been investigated for ethylbenzene: Activated Carbon.
[USEPA; Management of Hazardous Waste Leachate, EPA Contract No.68-03-2766 p.E-146 (1982)]**PEER REVIEWED**

The following wastewater treatment technologies have been investigated for ethylbenzene: biological treatment.
[USEPA; Management of Hazardous Waste Leachate, EPA Contract No.68-03-2766 p.E-45 (1982)]**PEER REVIEWED**

The following wastewater treatment technologies have been investigated for ethylbenzene: stripping.
[USEPA; Management of Hazardous Waste Leachate, EPA Contract No.68-03-2766 p.E-96 (1982)]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

DOT Emergency Guidelines:

Fire or explosion: Highly flammable: Will be easily ignited by heat, sparks or flames. Vapors may form explosive mixtures with air. Vapors may travel to source of ignition and flash back. Most vapors are heavier than air. They will spread along ground and collect in low confined areas (sewers, basements, tanks). Vapor explosion hazard indoors, outdoors or in sewers. Some may polymerize (P) explosively when heated or involved in a fire. Runoff to sewer may create fire or explosion hazard. Containers may explode when heated. Many liquids are lighter than water.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

Health: May cause toxic effects if inhaled or absorbed through skin. Inhalation or contact with material may irritate or burn skin and eyes. Fire will produce irritating, corrosive and/or toxic gases. Vapors may cause dizziness or suffocation. Runoff from fire control or dilution water may cause pollution.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

Public safety: Call Emergency Response Telephone Number. ... Isolate spill or leak area immediately for at least 50 to lOO meters (160 to 330 feet) in all directions. Keep unauthorized personnel away. Stay upwind. Keep out of low areas. Ventilate closed spaces before entering.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

Protective clothing: Wear positive pressure self-contained breathing apparatus (SCBA). Structural firefighters' protective clothing will only provide limited protection.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

Evacuation: Large spill: Consider initial downwind evacuation for at least 300 meters (1000 feet). Fire: If tank, rail car or tank truck is involved in a fire, isolate for 800 meters (1/2 mile) in all directions; also, consider initial evacuation for 800 meters (1/2 mile) in all directions.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

Fire: Caution: All these products have a very low flash point: Use of water spray when fighting fire may be inefficient. Small fires: Dry chemical, CO2, water spray or alcohol-resistant foam. Do not use dry chemical extinguishers to control fires involving nitromethane or nitroethane. Large fires: Water spray, fog or alcohol-resistant foam. Do not use straight streams. Move containers from fire area if you can do it without risk. Fire involving tanks or car/trailer loads: Fight fire from maximum distance or use unmanned hose holders or monitor nozzles. Cool containers with flooding quantities of water until well after fire is out. Withdraw immediately in case of rising sound from venting safety devices or discoloration of tank. Always stay away from the ends of tanks. For massive fire, use unmanned hose holders or monitor nozzles; if this is impossible, withdraw from area and let fire burn.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

Spill or leak: Eliminate all ignition sources (no smoking, flares, sparks or flames in immediate area). All equipment used when handling the product must be grounded. Do not touch or walk through spilled material. Stop leak if you can do it without risk. Prevent entry into waterways, sewers, basements or confined areas. A vapor suppressing foam may be used to reduce vapors. Absorb or cover with dry earth, sand or other non-combustible material and transfer to containers. Use clean non-sparking tools to collect absorbed material. Large spills: Dike far ahead of liquid spill for later disposal. Water spray may reduce vapor; but may not prevent ignition in closed spaces.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

First aid: Move victim to fresh air. Call emergency medical care. Apply artificial respiration if victim is not breathing. Administer oxygen if breathing is difficult. Remove and isolate contaminated clothing and shoes. In case of contact with substance, immediately flush skin or eyes with running water for at least 20 minutes. Wash skin with soap and water. Keep victim warm and quiet. Effects of exposure (inhalation, ingestion or skin contact) to substance may be delayed. Ensure that medical personnel are aware of the material(s) involved, and take precautions to protect themselves.
[U.S. Department of Transportation. 1996 North American Emergency

Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-129]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Odor Threshold:

140 ppm /Purity not specified/

[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

2-2.6 mg/cu m; detection: 0.4 mg/cu m /Purity not specified/

[Verschueren, K. Handbook of Environmental Data on Organic Chemicals. 3rd ed. New York, NY: Van Nostrand Reinhold Co., 1996. 944]**PEER REVIEWED**

Odor Low: 8.7 mg/cu m, Odor High: 870.0 mg/cu m

[Ruth JH; Am Ind Hyg Assoc J 47: A-142-51 (1986)]**PEER REVIEWED**

ETHYLBENZENE

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For other data, click on the Table of Contents

Fire Potential:

A very dangerous fire ... hazard when exposed to heat or flame ...
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1522]**PEER REVIEWED**

Electrical ignition hazard: May be ignited by static discharge.
[Environment Canada; Tech Info for Problem Spills: Ethylbenzene (Draft) p.4 (1982)]**PEER REVIEWED**

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NFPA Hazard Classification:

Health: 2. 2= Materials that, on intense or continued (but not chronic) exposure, could cause temporary incapacitation or possible residual injury, including those requiring the use of respiratory protective equipment that has an independent air supply. These materials are hazardous to health, but areas may be entered freely if personnel are provided with full-face mask self-contained breathing apparatus that provides complete eye protection.
[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 325-48]**PEER REVIEWED**

Flammability: 3. 3= This degree includes Class IB and IC flammable liquids and materials that can be easily ignited under almost all normal temperature conditions. Water may be ineffective in controlling or extinguishing fires in such materials.
[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 325-48]**PEER REVIEWED**

Reactivity: 0. 0= This degree includes materials that are normally stable, even under fire exposure conditions, and that do not react with water. Normal fire fighting procedures may be used.
[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 325-48]**PEER REVIEWED**

ETHYLBENZENE

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For other data, click on the Table of Contents

Flammable Limits:

Lower flammable limit: 0.8% by volume; Upper flammable limit: 6.7% by volume

[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 325-48]**PEER REVIEWED**

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CASRN: 100-41-4

For other data, click on the Table of Contents

Flash Point:

12.8 DEG C (55 DEG F) (CLOSED CUP)

[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1304]**PEER REVIEWED**

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CASRN: 100-41-4

For other data, click on the Table of Contents

Autoignition Temperature:

810 DEG F

[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1522]**PEER REVIEWED**

ETHYLBENZENE

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For other data, click on the Table of Contents

Fire Fighting Procedures:

Approach fire from upwind to avoid hazardous vapors and toxic decomposition products. Use water spray, dry chemical, foam, or carbon dioxide. Use water spray to keep fire-exposed containers cool. [Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 49-65]**PEER REVIEWED**

If material on fire or involved in fire: Do not extinguish fire unless flow can be stopped or safely confined. Use water in flooding quantities as fog. Solid streams of water may spread fire. Cool all affected containers with flooding quantities of water. Apply water from as far a distance as possible. Use foam, carbon dioxide, or dry chemical. [Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 443]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Toxic Combustion Products:

Irritating vapors are generated when heated.
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

The combustion products of ethylbenzene are water and carbon dioxide or carbon monoxide in limited oxygen atmospheres.
[Environment Canada; Tech Info for Problem Spills: Ethylbenzene (Draft) p.79 (1982)]**PEER REVIEWED**

Compounds identified in tars produced by the pyrolysis of ethylbenzene include the following suspected carcinogens: 1-benzanthracene, benzene, benzofluoranthene, 10,11-benzofluoranthene, 12-benzofluoranthene, 1-benzofluoranthene, 1-benzopyrene, 3,4-benzopyrene, chrysene, and 1,2:5,6-dibenzanthracene.
[NAS; The Alkylbenzenes p.99 (1981)]**PEER REVIEWED**

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For other data, click on the Table of Contents

Firefighting Hazards:

Vapors are heavier than air and may travel to a source of ignition and flash back. Liquid floats on water and may travel to a source of ignition and spread fire.

[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 49-65]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Explosive Limits & Potential:

Vapors form explosive mixtures with air.
[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 49-65]**PEER REVIEWED**

Lower explosive limit= 1.2%. Upper explosive limit= 6.8%.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1522]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Hazardous Reactivities & Incompatibilities:

Incompatibilities: Strong oxidizers.

[Sittig, M. Handbook of Toxic and Hazardous Chemicals and Carcinogens, 1985. 2nd ed. Park Ridge, NJ: Noyes Data Corporation, 1985. 4122]**PEER REVIEWED**

... Can react vigorously with oxidizing materials.

[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1522]**PEER REVIEWED**

Strong oxidizers.

[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 132]**PEER REVIEWED**

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For other data, click on the Table of Contents

Hazardous Decomposition:

When heated to decomposition it emits acrid smoke and irritating fumes.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 1522]**PEER REVIEWED**

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For other data, click on the Table of Contents

Immediately Dangerous to Life or Health:

800 ppm

[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 132]**PEER REVIEWED**

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For other data, click on the Table of Contents

Protective Equipment & Clothing:

Wear full protective clothing and positive pressure self-contained breathing apparatus.
[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 49-65]**PEER REVIEWED**

Rubber overclothing (including gloves)
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Wear appropriate personal protective clothing to prevent skin contact.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 132]**PEER REVIEWED**

Wear appropriate eye protection to prevent eye contact.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 132]**PEER REVIEWED**

Recommendations for respirator selection. Max concn for use: 800 ppm. Respirator Class(es): Any chemical cartridge respirator with organic vapor cartridge(s). May require eye protection. Any air-purifying, full-facepiece respirator (gas mask) with a chin-style, front- or back-mounted organic vapor canister. Any powered, air-purifying respirator with organic vapor cartridge(s). May require eye protection. Any supplied-air respirator. May require eye protection. Any self-contained breathing apparatus with a full facepiece.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 132]**PEER REVIEWED**

Recommendations for respirator selection. Condition: Emergency or planned entry into unknown concn or IDLH conditions: Respirator Class(es): Any self-contained breathing apparatus that has a full facepiece and is operated in a pressure-demand or other positive-pressure mode. Any supplied-air respirator that has a full facepiece and is operated in a pressure-demand or other positive-pressure mode in combination with an auxiliary self-contained breathing apparatus operated in pressure-demand or other positive-pressure mode.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 132]**PEER REVIEWED**

Recommendations for respirator selection. Condition: Escape from suddenly occurring respiratory hazards: Respirator Class(es): Any air-purifying, full-facepiece respirator (gas mask) with a chin-style, front- or back-mounted organic vapor canister. Any appropriate escape-type, self-contained breathing

apparatus.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 132]**PEER REVIEWED**

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For other data, click on the Table of Contents

Preventive Measures:

Contact lenses should not be worn when working with this chemical.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 132]**PEER REVIEWED**

SRP: The scientific literature for the use of contact lenses in industry is conflicting. The benefit or detrimental effects of wearing contact lenses depend not only upon the substance, but also on factors including the form of the substance, characteristics and duration of the exposure, the uses of other eye protection equipment, and the hygiene of the lenses. However, there may be individual substances whose irritating or corrosive properties are such that the wearing of contact lenses would be harmful to the eye. In those specific cases, contact lenses should not be worn. In any event, the usual eye protection equipment should be worn even when contact lenses are in place.
PEER REVIEWED

Employees should wash promptly when skin is wet or contaminated. Remove clothing immediately if wet or contaminated to avoid flammability hazard.
[Sittig, M. Handbook of Toxic and Hazardous Chemicals and Carcinogens, 1985. 2nd ed. Park Ridge, NJ: Noyes Data Corporation, 1985. 414]**PEER REVIEWED**

BEFORE WORKERS ARE ALLOWED TO ENTER A REACTION VESSEL ... THE VESSEL SHOULD BE PURGED AND WELL VENTILATED. PERSONAL PROTECTIVE EQUIPMENT SHOULD BE SUPPLIED ...
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 2114]**PEER REVIEWED**

... SUBSTITUTION OF LESS IRRITATING SUBSTANCES, ... REDESIGN OF OPERATIONS, ... PREVENT CONTACT, PROVISION OF A PHYSICAL BARRIER AGAINST CONTACT, PROPER WASHING FACILITIES, PROPER WORK CLOTHING AND STORAGE FACILITIES, PROTECTIVE CLOTHING, BARRIER CREAMS, AND MEDICAL CONTROL ...
[Sax, N.I. Dangerous Properties of Industrial Materials. 4th ed. New York: Van Nostrand Reinhold, 1975. 727]**PEER REVIEWED**

Personnel protection: Avoid breathing vapors. Keep upwind. ... Do not handle broken packages without protective equipment. Wash away any material which may have contacted the body with copious amounts of water or soap and water.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 443]**PEER REVIEWED**

COMBUSTION MAY BE IMPROVED BY MIXING WITH MORE FLAMMABLE LIQ. ... SHOULD

NOT BE ALLOWED TO ENTER CONFINED SPACE, SUCH AS SEWER, BECAUSE OF POSSIBILITY OF EXPLOSION.
[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) PublicationNo. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981. 2]**PEER REVIEWED**

If material not on fire and not involved in fire: Keep sparks, flames, and other sources of ignition away. Keep material out of water sources and sewers. Build dikes to contain flow as necessary. Attempt to stop leak if without hazard. Use water spray to knock-down vapors.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 443]**PEER REVIEWED**

The worker should immediately wash the skin when it becomes contaminated.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 132]**PEER REVIEWED**

Work clothing that becomes wet should be immediately removed due to its flammability hazard.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 132]**PEER REVIEWED**

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For other data, click on the Table of Contents

Shipment Methods and Regulations:

No person may /transport,/ offer or accept a hazardous material for transportation in commerce unless that person is registered in conformance ... and the hazardous material is properly classed, described, packaged, marked, labeled, and in condition for shipment as required or authorized by ... /the hazardous materials regulations (49 CFR 171-177)./

[49 CFR 171.2 (7/1/99)]**PEER REVIEWED**

The International Air Transport Association (IATA) Dangerous Goods Regulations are published by the IATA Dangerous Goods Board pursuant to IATA Resolutions 618 and 619 and constitute a manual of industry carrier regulations to be followed by all IATA Member airlines when transporting hazardous materials.

[IATA. Dangerous Goods Regulations. 40th Ed. Montreal, Canada and Geneva, Switzerland: International Air Transport Association, Dangerous Goods Regulations, 1999. 149]**PEER REVIEWED**

The International Maritime Dangerous Goods Code lays down basic principles for transporting hazardous chemicals. Detailed recommendations for individual substances and a number of recommendations for good practice are included in the classes dealing with such substances. A general index of technical names has also been compiled. This index should always be consulted when attempting to locate the appropriate procedures to be used when shipping any substance or article.

[IMDG; International Maritime Dangerous Goods Code; International Maritime Organization p.3222 (1998)]**PEER REVIEWED**

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Storage Conditions:

Outside or detached storage is preferred. Inside storage should be in a standard flammable liquids storage warehouse, room, or cabinet. Separate from oxidizing materials.
[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 49-65]**PEER REVIEWED**

Temp: ambient; Venting: open (flame arrester) or pressure-vacuum
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

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Cleanup Methods:

1) REMOVE ALL IGNITION SOURCES. 2) VENTILATE AREA OF SPILL OR LEAK. 3) FOR SMALL QUANTITIES, ABSORB ON PAPER TOWELS. EVAPORATE IN SAFE PLACE (SUCH AS FUME HOOD). ... BURN PAPER IN SUITABLE LOCATION AWAY FROM COMBUSTIBLE MATERIALS. LARGE QUANTITIES CAN BE COLLECTED & ATOMIZED IN SUITABLE COMBUSTION CHAMBER.
[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) PublicationNo. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981. 1]**PEER REVIEWED**

Land spills should be contained; skimming equipment and/or sorbent (polyurethane) foams can be used. Use of activated carbon is recommended.
[Environment Canada; Tech Info for Problem Spills: Ethylbenzene p.83 (1982)]**PEER REVIEWED**

Water spills should be contained; skimming equipment and/or sorbent (polyurethane) foams can be used to remove the slick. Universal gelling agent can be used to solidify a trapped mass. Use of activated carbon on dissolved portion is recommended.
[Environment Canada; Tech Info for Problem Spills: Ethylbenzene p.83 (1982)]**PEER REVIEWED**

Environmental considerations: Land spill: Dig a pit, pond, lagoon, or holding area to contain liquid or solid material. /SRP: If time permits, pits, ponds, lagoons, soak holes, or holding areas should be sealed with an impermeable flexible membrane liner./ Dike surface flow using sand bags, foamed polyurethane, or foamed concrete. Absorb bulk liquid with fly ash, cement powder, sawdust, or commercial sorbents. Apply "universal" gelling agent to immobilize spill. Apply appropriate foam to diminish vapor and fire hazard.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 443]**PEER REVIEWED**

Environmental considerations - Air spill: Apply water spray or mist to knock down vapors.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 443]**PEER REVIEWED**

Environmental considerations: Water spill: Use natural barriers or oil spill control booms to limit spill travel. Use surface active agent (e.g., detergent, soaps, alcohols), if approved by EPA. Inject "universal" gelling agent to solidify encircled spill and increase effectiveness of booms. If dissolved, in region of 10 ppm or greater concentration, apply activated carbon at ten times the spilled amount. Remove trapped material with suction hoses. Use mechanical dredges or lifts to remove immobilized masses of pollutants and precipitates.

[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 443]**PEER REVIEWED**

ABSORB IN VERMICULITE, DRY SAND, EARTH OR SIMILAR MATERIAL
[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) PublicationNo. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981. 2]**PEER REVIEWED**

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For other data, click on the Table of Contents

Disposal Methods:

Generators of waste (equal to or greater than 100 kg/mo) containing this contaminant, EPA hazardous waste number F003, must conform with USEPA regulations in storage, transportation, treatment and disposal of waste.
[40 CFR 240-280, 300-306, 702-799 (7/1/90)]**PEER REVIEWED**

Ethylbenzene is a waste chemical stream constituent which may be subjected to ultimate disposal by controlled incineration.
[USEPA; Engineering Handbook for Hazardous Waste Incineration p.2-6 (1981) EPA 68-03-3025]**PEER REVIEWED**

A good candidate for liquid injection incineration at a temperature range of 650 to 1,600 deg C and a residence time of 0.1 to 2 seconds. A good candidate for rotary kiln incineration at a temperature range of 820 to 1,600 deg C and residence times of seconds for liquids and gases, and hours for solids. A good candidate for fluidized bed incineration at a temperature range of 450 to 980 deg C and residence times of seconds for liquids and gases, and longer for solids.
[USEPA; Engineering Handbook for Hazardous Waste Incineration p.3-4 (1981) EPA 68-03-3025]**PEER REVIEWED**

The following wastewater treatment technologies have been investigated for ethylbenzene: Activated Carbon.
[USEPA; Management of Hazardous Waste Leachate, EPA Contract No.68-03-2766 p.E-146 (1982)]**PEER REVIEWED**

The following wastewater treatment technologies have been investigated for ethylbenzene: biological treatment.
[USEPA; Management of Hazardous Waste Leachate, EPA Contract No.68-03-2766 p.E-45 (1982)]**PEER REVIEWED**

The following wastewater treatment technologies have been investigated for ethylbenzene: stripping.
[USEPA; Management of Hazardous Waste Leachate, EPA Contract No.68-03-2766 p.E-96 (1982)]**PEER REVIEWED**

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For other data, click on the Table of Contents

Occupational Exposure Standards:

OSHA Standards:

Permissible Exposure Limit: Table Z-1 8-Hr Time Weighted Avg: 100 ppm (435 mg/cu m).
[29 CFR 1910.1000 (7/1/99)]**PEER REVIEWED**

Vacated 1989 OSHA PEL TWA 100 ppm (435 mg/cu m); STEL 125 ppm (545 mg/cu m) is still enforced in some states.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 364]**PEER REVIEWED**

Threshold Limit Values:

8 Hr Time Weighted Avg (TWA) 100 ppm; Short Term Exposure Limit (STEL) 125 ppm
[American Conference of Governmental Industrial Hygienists. Threshold Limit Values (TLVs) for Chemical Substances and Physical Agents Biological Exposure Indices for 1998. Cincinnati, OH: ACGIH, 1998. 37]**PEER REVIEWED**

BEI (Biological Exposure Index): Biological Exposure Index (BEI) adoption (1986 edition): Determinant: Mandelic acid in urine; Sampling Time: end of shift at end of workweek; BEI: 1.5 g/g creatinine. The determinant is nonspecific, since it is observed after exposure to some other chemicals. These nonspecific tests are preferred because they are easy to use and usually offer a better correlation with exposure than specific tests. In such instances, a BEI for a specific, less quantitative biological determinant is recommended as a confirmatory test.
[American Conference of Governmental Industrial Hygienists. Threshold Limit Values (TLVs) for Chemical Substances and Physical Agents Biological Exposure Indices for 1998. Cincinnati, OH: ACGIH, 1998. 100]**PEER REVIEWED**

BEI (Biological Exposure Index): Determinant: Ethyl benzene in end-exhaled air . The biological determinant is an indicator of exposure to the chemical, but the quantitative interpretation of the measurements is ambiguous. (1986 adoption)
[American Conference of Governmental Industrial Hygienists. Threshold Limit Values (TLVs) for Chemical Substances and Physical Agents Biological Exposure Indices for 1998. Cincinnati, OH: ACGIH, 1998. 100]**PEER REVIEWED**

NIOSH Recommendations:

Recommended Exposure Limit: 10 Hr Time-Weighted Avg: 100 ppm (435 mg/cu m).
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing

Office, 1997. 132]**PEER REVIEWED**

Recommended Exposure Limit: 15 Min Short-Term Exposure Limit: 125 ppm (545 mg/cu m).
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 132]**PEER REVIEWED**

Immediately Dangerous to Life or Health:

800 ppm
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 132]**PEER REVIEWED**

Other Occupational Permissible Levels:

Australia: 100 ppm, STEL 125 ppm, substance under review (1990); Federal Republic of Germany: 100 ppm, short-term level 200 ppm, 5 min, 8 times per shift, skin (1990); Sweden: 80 ppm, short-term value 100 ppm, 15 min (1989); United Kingdom: 100 ppm, 10-min STEL 125 ppm (1991).
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Volumes I,II, III. Cincinnati, OH: ACGIH, 1991. 584]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

OSHA Standards:

Permissible Exposure Limit: Table Z-1 8-Hr Time Weighted Avg: 100 ppm (435 mg/cu m).
[29 CFR 1910.1000 (7/1/99)]**PEER REVIEWED**

Vacated 1989 OSHA PEL TWA 100 ppm (435 mg/cu m); STEL 125 ppm (545 mg/cu m) is still enforced in some states.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 364]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Threshold Limit Values:

8 Hr Time Weighted Avg (TWA) 100 ppm; Short Term Exposure Limit (STEL) 125 ppm
[American Conference of Governmental Industrial Hygienists. Threshold Limit Values (TLVs) for Chemical Substances and Physical Agents Biological Exposure Indices for 1998. Cincinnati, OH: ACGIH, 1998. 37]**PEER REVIEWED**

BEI (Biological Exposure Index): Biological Exposure Index (BEI) adoption (1986 edition): Determinant: Mandelic acid in urine; Sampling Time: end of shift at end of workweek; BEI: 1.5 g/g creatinine. The determinant is nonspecific, since it is observed after exposure to some other chemicals. These nonspecific tests are preferred because they are easy to use and usually offer a better correlation with exposure than specific tests. In such instances, a BEI for a specific, less quantitative biological determinant is recommended as a confirmatory test.
[American Conference of Governmental Industrial Hygienists. Threshold Limit Values (TLVs) for Chemical Substances and Physical Agents Biological Exposure Indices for 1998. Cincinnati, OH: ACGIH, 1998. 100]**PEER REVIEWED**

BEI (Biological Exposure Index): Determinant: Ethyl benzene in end-exhaled air . The biological determinant is an indicator of exposure to the chemical, but the quantitative interpretation of the measurements is ambiguous. (1986 adoption)
[American Conference of Governmental Industrial Hygienists. Threshold Limit Values (TLVs) for Chemical Substances and Physical Agents Biological Exposure Indices for 1998. Cincinnati, OH: ACGIH, 1998. 100]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

NIOSH Recommendations:

Recommended Exposure Limit: 10 Hr Time-Weighted Avg: 100 ppm (435 mg/cu m).
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 132]**PEER REVIEWED**

Recommended Exposure Limit: 15 Min Short-Term Exposure Limit: 125 ppm (545 mg/cu m).
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 132]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Other Occupational Permissible Levels:

Australia: 100 ppm, STEL 125 ppm, substance under review (1990); Federal Republic of Germany: 100 ppm, short-term level 200 ppm, 5 min, 8 times per shift, skin (1990); Sweden: 80 ppm, short-term value 100 ppm, 15 min (1989); United Kingdom: 100 ppm, 10-min STEL 125 ppm (1991).
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Volumes I,II, III. Cincinnati, OH: ACGIH, 1991. 584]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Manufacturing/Use Information:

Major Uses:

USED IN ... THE PRODUCTION OF SYNTHETIC RUBBER ... AS A SOLVENT OR DILUENT, A COMPONENT OF AUTOMOTIVE AND AVIATION FUELS; MFR OF CELLULOSE ACETATE
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 2114]**PEER REVIEWED**

Ethylbenzene is mainly used as a precursor to styrene.
[Kirk-Othmer Encyclopedia of Chemical Technology. 4th ed. Volumes 1: New York, NY. John Wiley and Sons, 1991-Present.,p. V2 84]**PEER REVIEWED**

... SOLVENT-EG, FOR ALKYD SURFACE COATINGS, CHEM INT FOR DIETHYLBENZENE & ACETOPHENONE, FOR ETHYL ANTHRAQUINONE, FOR ETHYLBENZENE SULFONIC ACIDS (O-, M- & P-), FOR PROPYLENE OXIDE & ALPHA-METHYLBENZYL ALCOHOL, UNRECOVERED COMPONENT OF GASOLINE
[SRI]**PEER REVIEWED**

Used as an intermediate for the manufacture of the styrene monomer and as a resin solvent.
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 643]**PEER REVIEWED**

Intermediate for the production of diethylbenzene and acetophenone.
[Gerhartz, W. (exec ed.). Ullmann's Encyclopedia of Industrial Chemistry. 5th ed.Vol A1: Deerfield Beach, FL: VCH Publishers, 1985 to Present.,p. VA10 35]**PEER REVIEWED**

Used as a component of automotive and aviation fuels.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1342]**PEER REVIEWED**

Intermediate in production of styrene solvent.
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 1997. 461]**PEER REVIEWED**

Manufacturers:

Amoco Corporation, Hq, 200 East Randolph Drive, Chicago, IL 60601, (312) 856-6111; Subsidiary: Amoco Chemical Company (address same as Hq), (312) 856-3200; Chemical & Specialty Product Group; Production site: Texas City, TX 77592

[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 593]**PEER REVIEWED**

ARCO Chemical Co., Hq, 3801 W. Chester Pk., Newtown Square, PA 19073; Production site: Channelview, TX 77530
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 583]**PEER REVIEWED**

Chevron Chemical Co., 6001 Bollinger Canyon Rd., San Ramon, CA 94583, (925) 842-5500; Production site: St. James, LA 70086
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 593]**PEER REVIEWED**

Cos-Mar, Inc., Hq, PO Box 11, Carville, LA 70721, (504) 642-5454; Production site: Carville, LA 70721
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 593]**PEER REVIEWED**

Dow Chemical USA, Hq, 2020 Dow Center, Midland, MI 48674, (517) 636-1000; Production site: Freeport, TX 77541
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 593]**PEER REVIEWED**

Huntsman Corp., 3040 Post Oak Blvd., Houston, TX 77056, (713) 235-6000; Production site: Odessa, TX 79760
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 593]**PEER REVIEWED**

Sterling Chemicals, Inc., Hq, 333 Clay St., Suite 3700, Houston, TX 77002, (713) 650-3700; Production site: Texas City, TX 77590
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 593]**PEER REVIEWED**

Westlake Styrene Corp., 2801 Post Oak Blvd., Suite 200, Houston, TX 77056, (713) 877-1924; Production site: Lake Charles, LA 70602-3089
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 593]**PEER REVIEWED**

Methods of Manufacturing:

Prepared by dehydrogenation of naphthenes or from catalytic cyclization and aromatization.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1342]**PEER REVIEWED**

ALKYLATION OF BENZENE WITH ETHYLENE IN LIQUID PHASE USING ALUMINUM CHLORIDE CATALYST OR IN VAPOR PHASE USING PHOSPHORIC ACID OR ALUMINA-SILICA CATALYST; RECOVERY FROM MIXED XYLENES VIA FRACTIONATION
[SRI]**PEER REVIEWED**

Prepd from acetophenone

[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 643]**PEER REVIEWED**

Produced by alkylation of benzene with ethylene using acidic catalysts and can be carried out in the liquid or vapor phase.
[Kirk-Othmer Encyclopedia of Chemical Technology. 4th ed. Volumes 1: New York, NY. John Wiley and Sons, 1991-Present.,p. V22 957]**PEER REVIEWED**

Produced via the use of zeolite catalyst, ZSM-5, in a process called the Mobil-Badger vapor phase ethylbenzene process.
[Kirk-Othmer Encyclopedia of Chemical Technology. 4th ed. Volumes 1: New York, NY. John Wiley and Sons, 1991-Present.,p. V22 961]**PEER REVIEWED**

(1) By heating benzene and ethylene in the presence of aluminum chloride, with subsequent distillation; (2) by fractionation directly from the mixed xylene stream in petroleum refining.
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 1997. 461]**PEER REVIEWED**

General Manufacturing Information:

In most processes, ethylbenzene is not recovered because of high energy costs.
[Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984.,p. V24 717 (1983)]**PEER REVIEWED**

Ethylbenzene is recovered from benzene-toluene-xylene (BTX) processing.
[Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984.,p. V4 64 (1978)]**PEER REVIEWED**

19th-highest-volume chemical produced in the U.S. (1995).
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 1997. 461]**PEER REVIEWED**

Formulations/Preparations:

GRADE: TECHNICAL 99.0%; PURE 99.5%; RESEARCH 99.98%.
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Grade: Technical, pure, research
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 1997. 461]**PEER REVIEWED**

Consumption Patterns:

Intermediate for styrene monomer production, more than 99%; the remainder is exported or sold as solvent (1984).
[CHEMICAL PROFILE: Ethylbenzene, 1984]**PEER REVIEWED**

Styrene, 97%; Miscellaneous, 3% (1983) /Estimate/
[CHEMICAL PRODUCTS SYNOPSIS: Ethylbenzene, 1983]**PEER REVIEWED**

CHEMICAL PROFILE: Ethylbenzene. Intermediate for styrene monomer production, over 99%. The remainder is used in solvent applications.
[Kavaler AR; Chemical Marketing Reporter 236 (8): 50 (1989)]**PEER REVIEWED**

CHEMICAL PROFILE: Ethylbenzene. Demand: 1988: 9,935 million lb; 1989: 10,230 million lb; 1993 /projected/: 11,500 million lb. (Imports and exports are both minor, each one on the order of 200 million lb.)
[Kavaler AR; Chemical Marketing Reporter 236 (8): 50 (1989)]**PEER REVIEWED**

Precursors for styrene production, more than 99 percent. The remainder is used in solvent applications.
[Chemical Marketing Reporter; Chemical Profile Ethylbenzene. April 27, 1998. p. 57. NY,NY: Schnell Pub Co (1998)]**PEER REVIEWED**

U. S. Production:

(1977) 8.3X10+9 lb
[United States International Trade Commission. Synthetic Organic Chemicals-- United States Production and Sales, 1981. USITC Publications 1291 Washington, DC: United States InternationalTrade Commission, 1981. 27]**PEER REVIEWED**

(1980) 3.5 x 10+12 g
[Kavaler, A.R. (ed.). Chemical Marketing Reporter. New York, NY: Schnell Publishing Co., Inc., 1984]**PEER REVIEWED**

(1981) 3.5 x 10+12 g
[Kavaler, A.R. (ed.). Chemical Marketing Reporter. New York, NY: Schnell Publishing Co., Inc., 1984]**PEER REVIEWED**

(1977) 3.77X10+12 G
[SRI]**PEER REVIEWED**

(1982) 3.15X10+12 G
[SRI]**PEER REVIEWED**

(1985) 3.35X10+12 g
[USITC, SYN ORG CHEM-US PROD/SALES (1985) p.29]**PEER REVIEWED**

(1988) 9.9X10+9 lb
[United States International Trade Commission. Synthetic Organic Chemicals- United States Production and Sales, 1988. USITC Publication

1989. Washington,DC: United States International Trade Commission, 1989.,p. 3-2]**PEER REVIEWED**

(1990) 8.37 billion lb
[Chem & Engineering News 70 (15): 17 (4/13/92)]**PEER REVIEWED**

(1991) 8.87 billion lb
[Chem & Engineering News 71 (15): 11 (4/12/93)]**PEER REVIEWED**

(1992) 11.11 billion lb
[Chem & Engineering News 72 (15): 13 (4/11/94)]**PEER REVIEWED**

(1993) 11.76 billion lb
[Chem & Engineering News 72 (15): 13 (4/11/94)]**PEER REVIEWED**

(1993) 4,233,835 kg
[United States International Trade Commission. Synthetic Organic Chemicals - United States Production and Sales, 1993. USITC Publication 2810, Nov. 1994. Washington, D.C.,p. 3-15]**PEER REVIEWED**

1997: 12.9 billion pounds; 1998 13 billion pounds; 2002 15 billion pounds. (Includes exports, which amounted to 126 million pounds in 1996, but not imports which totaled 16 million pounds in that year).
[Chemical Marketing Reporter; Chemical Profile Ethylbenzene. April 27, 1998. p. 57. NY,NY: Schnell Pub Co (1998)]**PEER REVIEWED**

Growth: Historical (1988-1997): 2.5 percent per year; future: 3 percent per year through 2002.
[Chemical Marketing Reporter; Chemical Profile Ethylbenzene. April 27, 1998. p. 57. NY,NY: Schnell Pub Co (1998)]**PEER REVIEWED**

U. S. Imports:

(1978) 1.53X10+10 G
[SRI]**PEER REVIEWED**

(1981) 2.09X10+10 G
[SRI]**PEER REVIEWED**

US General Imports entered under schedule 4, pt 1B, of the TSUS (1983). Quantity of ethylbenzene: 87,201,615 lbs.
[USITC. IMPORTS OF BENZENOID CHEM & PROD (1983) p.18]**PEER REVIEWED**

(1996) 16 million pounds
[Chemical Marketing Reporter; Chemical Profile Ethylbenzene. April 27, 1998. p. 57. NY,NY: Schnell Pub Co (1998)]**PEER REVIEWED**

U. S. Exports:

(1978) 8.59X10+10 G
[SRI]**PEER REVIEWED**

(1983) 4.84X10+10 G
[SRI]**PEER REVIEWED**

(1985) 7.49X10+10 g
[BUREAU OF THE CENSUS, US EXPORTS, SCHEDULE E, (1985) p.2-69]**PEER REVIEWED**

(1996) 126 million pounds
[Chemical Marketing Reporter; Chemical Profile Ethylbenzene. April 27, 1998. p. 57. NY,NY: Schnell Pub Co (1998)]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Major Uses:

USED IN ... THE PRODUCTION OF SYNTHETIC RUBBER ... AS A SOLVENT OR DILUENT, A COMPONENT OF AUTOMOTIVE AND AVIATION FUELS; MFR OF CELLULOSE ACETATE
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 2114]**PEER REVIEWED**

Ethylbenzene is mainly used as a precursor to styrene.
[Kirk-Othmer Encyclopedia of Chemical Technology. 4th ed. Volumes 1: New York, NY. John Wiley and Sons, 1991-Present.,p. V2 84]**PEER REVIEWED**

... SOLVENT-EG, FOR ALKYD SURFACE COATINGS, CHEM INT FOR DIETHYLBENZENE & ACETOPHENONE, FOR ETHYL ANTHRAQUINONE, FOR ETHYLBENZENE SULFONIC ACIDS (O-, M- & P-), FOR PROPYLENE OXIDE & ALPHA-METHYLBENZYL ALCOHOL, UNRECOVERED COMPONENT OF GASOLINE
[SRI]**PEER REVIEWED**

Used as an intermediate for the manufacture of the styrene monomer and as a resin solvent.
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 643]**PEER REVIEWED**

Intermediate for the production of diethylbenzene and acetophenone.
[Gerhartz, W. (exec ed.). Ullmann's Encyclopedia of Industrial Chemistry. 5th ed.Vol A1: Deerfield Beach, FL: VCH Publishers, 1985 to Present.,p. VA10 35]**PEER REVIEWED**

Used as a component of automotive and aviation fuels.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1342]**PEER REVIEWED**

Intermediate in production of styrene solvent.
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 1997. 461]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Manufacturers:

Amoco Corporation, Hq, 200 East Randolph Drive, Chicago, IL 60601, (312) 856-6111; Subsidiary: Amoco Chemical Company (address same as Hq), (312) 856-3200; Chemical & Specialty Product Group; Production site: Texas City, TX 77592
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 593]**PEER REVIEWED**

ARCO Chemical Co., Hq, 3801 W. Chester Pk., Newtown Square, PA 19073; Production site: Channelview, TX 77530
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 583]**PEER REVIEWED**

Chevron Chemical Co., 6001 Bollinger Canyon Rd., San Ramon, CA 94583, (925) 842-5500; Production site: St. James, LA 70086
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 593]**PEER REVIEWED**

Cos-Mar, Inc., Hq, PO Box 11, Carville, LA 70721, (504) 642-5454; Production site: Carville, LA 70721
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 593]**PEER REVIEWED**

Dow Chemical USA, Hq, 2020 Dow Center, Midland, MI 48674, (517) 636-1000; Production site: Freeport, TX 77541
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 593]**PEER REVIEWED**

Huntsman Corp., 3040 Post Oak Blvd., Houston, TX 77056, (713) 235-6000; Production site: Odessa, TX 79760
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 593]**PEER REVIEWED**

Sterling Chemicals, Inc., Hq, 333 Clay St., Suite 3700, Houston, TX 77002, (713) 650-3700; Production site: Texas City, TX 77590
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 593]**PEER REVIEWED**

Westlake Styrene Corp., 2801 Post Oak Blvd., Suite 200, Houston, TX 77056, (713) 877-1924; Production site: Lake Charles, LA 70602-3089
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 593]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Methods of Manufacturing:

Prepared by dehydrogenation of naphthenes or from catalytic cyclization and aromatization.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1342]**PEER REVIEWED**

ALKYLATION OF BENZENE WITH ETHYLENE IN LIQUID PHASE USING ALUMINUM CHLORIDE CATALYST OR IN VAPOR PHASE USING PHOSPHORIC ACID OR ALUMINA-SILICA CATALYST; RECOVERY FROM MIXED XYLENES VIA FRACTIONATION
[SRI]**PEER REVIEWED**

Prepd from acetophenone
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 643]**PEER REVIEWED**

Produced by alkylation of benzene with ethylene using acidic catalysts and can be carried out in the liquid or vapor phase.
[Kirk-Othmer Encyclopedia of Chemical Technology. 4th ed. Volumes 1: New York, NY. John Wiley and Sons, 1991-Present.,p. V22 957]**PEER REVIEWED**

Produced via the use of zeolite catalyst, ZSM-5, in a process called the Mobil-Badger vapor phase ethylbenzene process.
[Kirk-Othmer Encyclopedia of Chemical Technology. 4th ed. Volumes 1: New York, NY. John Wiley and Sons, 1991-Present.,p. V22 961]**PEER REVIEWED**

(1) By heating benzene and ethylene in the presence of aluminum chloride, with subsequent distillation; (2) by fractionation directly from the mixed xylene stream in petroleum refining.
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 1997. 461]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

General Manufacturing Information:

In most processes, ethylbenzene is not recovered because of high energy costs.
[Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984.,p. V24 717 (1983)]**PEER REVIEWED**

Ethylbenzene is recovered from benzene-toluene-xylene (BTX) processing.
[Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984.,p. V4 64 (1978)]**PEER REVIEWED**

19th-highest-volume chemical produced in the U.S. (1995).
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 1997. 461]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Formulations/Preparations:

GRADE: TECHNICAL 99.0%; PURE 99.5%; RESEARCH 99.98%.
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Grade: Technical, pure, research
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 1997. 461]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Consumption Patterns:

Intermediate for styrene monomer production, more than 99%; the remainder is exported or sold as solvent (1984).
[CHEMICAL PROFILE: Ethylbenzene, 1984]**PEER REVIEWED**

Styrene, 97%; Miscellaneous, 3% (1983) /Estimate/
[CHEMICAL PRODUCTS SYNOPSIS: Ethylbenzene, 1983]**PEER REVIEWED**

CHEMICAL PROFILE: Ethylbenzene. Intermediate for styrene monomer production, over 99%. The remainder is used in solvent applications.
[Kavaler AR; Chemical Marketing Reporter 236 (8): 50 (1989)]**PEER REVIEWED**

CHEMICAL PROFILE: Ethylbenzene. Demand: 1988: 9,935 million lb; 1989: 10,230 million lb; 1993 /projected/: 11,500 million lb. (Imports and exports are both minor, each one on the order of 200 million lb.)
[Kavaler AR; Chemical Marketing Reporter 236 (8): 50 (1989)]**PEER REVIEWED**

Precursors for styrene production, more than 99 percent. The remainder is used in solvent applications.
[Chemical Marketing Reporter; Chemical Profile Ethylbenzene. April 27, 1998. p. 57. NY,NY: Schnell Pub Co (1998)]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

U. S. Production:

(1977) 8.3X10+9 lb
[United States International Trade Commission. Synthetic Organic Chemicals-- United States Production and Sales, 1981. USITC Publications 1291 Washington, DC: United States InternationalTrade Commission, 1981. 27]**PEER REVIEWED**

(1980) 3.5 x 10+12 g
[Kavaler, A.R. (ed.). Chemical Marketing Reporter. New York, NY: Schnell Publishing Co., Inc., 1984]**PEER REVIEWED**

(1981) 3.5 x 10+12 g
[Kavaler, A.R. (ed.). Chemical Marketing Reporter. New York, NY: Schnell Publishing Co., Inc., 1984]**PEER REVIEWED**

(1977) 3.77X10+12 G
[SRI]**PEER REVIEWED**

(1982) 3.15X10+12 G
[SRI]**PEER REVIEWED**

(1985) 3.35X10+12 g
[USITC, SYN ORG CHEM-US PROD/SALES (1985) p.29]**PEER REVIEWED**

(1988) 9.9X10+9 lb
[United States International Trade Commission. Synthetic Organic Chemicals- United States Production and Sales, 1988. USITC Publication 1989. Washington,DC: United States International Trade Commission, 1989.,p. 3-2]**PEER REVIEWED**

(1990) 8.37 billion lb
[Chem & Engineering News 70 (15): 17 (4/13/92)]**PEER REVIEWED**

(1991) 8.87 billion lb
[Chem & Engineering News 71 (15): 11 (4/12/93)]**PEER REVIEWED**

(1992) 11.11 billion lb
[Chem & Engineering News 72 (15): 13 (4/11/94)]**PEER REVIEWED**

(1993) 11.76 billion lb
[Chem & Engineering News 72 (15): 13 (4/11/94)]**PEER REVIEWED**

(1993) 4,233,835 kg
[United States International Trade Commission. Synthetic Organic Chemicals - United States Production and Sales, 1993. USITC

Publication 2810, Nov. 1994. Washington, D.C.,p. 3-15]**PEER REVIEWED**

1997: 12.9 billion pounds; 1998 13 billion pounds; 2002 15 billion pounds. (Includes exports, which amounted to 126 million pounds in 1996, but not imports which totaled 16 million pounds in that year).
[Chemical Marketing Reporter; Chemical Profile Ethylbenzene. April 27, 1998. p. 57. NY,NY: Schnell Pub Co (1998)]**PEER REVIEWED**

Growth: Historical (1988-1997): 2.5 percent per year; future: 3 percent per year through 2002.
[Chemical Marketing Reporter; Chemical Profile Ethylbenzene. April 27, 1998. p. 57. NY,NY: Schnell Pub Co (1998)]**PEER REVIEWED**

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U. S. Imports:

(1978) 1.53X10+10 G
[SRI]**PEER REVIEWED**

(1981) 2.09X10+10 G
[SRI]**PEER REVIEWED**

US General Imports entered under schedule 4, pt 1B, of the TSUS (1983). Quantity of ethylbenzene: 87,201,615 lbs.
[USITC. IMPORTS OF BENZENOID CHEM & PROD (1983) p.18]**PEER REVIEWED**

(1996) 16 million pounds
[Chemical Marketing Reporter; Chemical Profile Ethylbenzene. April 27, 1998. p. 57. NY,NY: Schnell Pub Co (1998)]**PEER REVIEWED**

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U. S. Exports:

(1978) 8.59X10+10 G
[SRI]**PEER REVIEWED**

(1983) 4.84X10+10 G
[SRI]**PEER REVIEWED**

(1985) 7.49X10+10 g
[BUREAU OF THE CENSUS, US EXPORTS, SCHEDULE E, (1985) p.2-69]**PEER REVIEWED**

(1996) 126 million pounds
[Chemical Marketing Reporter; Chemical Profile Ethylbenzene. April 27, 1998. p. 57. NY,NY: Schnell Pub Co (1998)]**PEER REVIEWED**

ETHYLBENZENE

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Laboratory Methods:

Clinical Laboratory Methods:

IN BLOOD BY ULTRAVIOLET-SPECTROPHOTOMETRIC METHOD.
[Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965. 91]**PEER REVIEWED**

An automated high performance liquid chromatographic method for the direct determination of urinary concentrations of phenyl glyoxylic acid and mandelic acid, metabolites of styrene or ethylbenzene, is described. The method is simple and specific. Urine can be analyzed without solvent extraction. Analysis can be performed satisfactorily within 15 minutes for samples containing hippuric acid, o-, m- and p-methyl hippuric acids, phenyl glyoxylic acid, and mandelic acid, and within 15 minutes for those containing hippuric acid, phenyl glyoxylic acid and mandelic acid.
[Ogata M, Taguchi T; Int Arch Occup Environ Health 59 (3): 263-72 (1987)]**PEER REVIEWED**

Analytic Laboratory Methods:

EPA Method 624. Purge-and-Trap Gas Chromatography/Mass Spectrometry for the analysis of purgeable organics including ethylbenzene in the municipal and industrial discharges. Under the prescribed conditions, for ethylbenzene the method has a detection limit of 7.2 ug/l. Precision and method accuracy were found to be directly related to the concentration of the analyte and essentially independent of the sample matrix.
[40 CFR 136 (7/1/91)]**PEER REVIEWED**

EPA Method 1624. Isotope Dilution Purge-and-Trap Gas Chromatography/Mass Spectrometry. This method is applicable for the determination of volatile organic compounds in municpal and industrial discharges. By adding a known amount of a labeled compound to every sample prior to purging, a correction of recovery of the pollutant can be made. If labeled compounds are not available, an internal standard method is used. Under the prescribed conditions, for both the labeled, and unlabeled ethylbenzene the method has a minimum detection level 10 ug/l.The established acceptance performance criteria at 20 ug/l is 9.6 ug/l for the standard deviation of the recovery, with the average recovery of 15.6 to 28.5 ug/l and the labeled cmpd recovery ranging from below detection to 203%.
[40 CFR 136 (7/1/91)]**PEER REVIEWED**

EPA Method 602. Purge-and-Trap Gas Chromatography with photoionization detection for the determination of purgeable aromatics including ethylbenzene in municipal and industrial discharges. Under the prescribed conditionss for ethylbenzene the detection limit is 0.2 ug/l. The method is applicable for use in the concentration range from the method detection limit to times that limit. Precision and method accuracy were found to be directly related to the concentration of the analyte essentially independent of the sample matrix.
[40 CFR 136 (7/1/91)]**PEER REVIEWED**

EPA Method 524.2. Purge-and-Trap Gas Chromatography/Mass Spectrometry for the determination of volatile aromatic compounds in water including finished drinking water, raw source water, and drinking water in any treatment stage. For ethylbenzene the method has a detection limit of 0.06 ug/l and a relative standard deviation of 8.6% with a wide bore capillary column, and a method detection limit of 0.03 ug/l and a relative standard deviation of 5.3% with a narrow bore capillary column.
[USEPA; Methods for the Determinatioon of Organic Compounds in Finished Drinking Water and Raw Source Water (19860]**PEER REVIEWED**

EPA Method 503.1. Purge-and-Trap Gas Chromatography with a Photoionization Detector. The method is applicable for the determination of volatile aromatic and unsaturated organic compounds in finished drinking water, raw source water, or drinking water in any treatment stage. For ethylbenzene the method has a detection limit of 0.002 ug/l and a relative standard deviation of 8.5%. Overall precision and method accuracy were found to be directly related to the concentration of the analyte essentially independent of sample matrix.
[USEPA; Methods for the Determination of Organic Compouds in Finished Drinking Water and Raw Source Water (1986)]**PEER REVIEWED**

EPA Method 502.2: Purge-and-Trap Capillary Column Gas Chromatography with Photoionization and Electrolytic Conductivity Detectors in Series. The method is applicable for the determination of volatile organic compounds in finished drinking water, raw source water, or drinking water in any treatment stage. For ethylbenzene the method has a detection limit of 0.005 ug/l, a percent recovery of 101%, and a standard deviation of 1.4 using the photoionization detector; and there is no data given for the following: the method detection limit, a percent recovery, or the standard deviation of recovery using the electrolytic conductivity detector.
[USEPA; Methods for the Determination of Organic Compounds in Finished Drinking Water and Raw Source Water (1986)]**PEER REVIEWED**

NIOSH Method 1501. Determination of Aromatic Hydrocarbons by Gas Chromatography with Flame Ionization Detection.
[U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSH Manual of Analytical Methods. 4th ed.Methods A-Z & Supplements. Washington, DC: U.S. Government Printing Office, Aug 1994.]**PEER REVIEWED**

EPA Method 8240. Gas Chromatography/Mass Spectrometry for the determination of volatile organics. This method can be used to quantify most volatile organic compounds including ethylbenzene that have boiling points below 200 deg C and are insoluble or slightly soluble in water. The detection limit is not given. Precision and method accuracy were found to be directly related to the concentration of the analyte and essentially independent of the sample matrix.
[USEPA/Office of Solid Waste (OSW); Test Methods for Evaluating Solid Waste, Physical/Chemical Methods SW846 Methods (1986)]**PEER REVIEWED**

EPA Method 8260. Gas Chromatography/Mass Spectrometry for the determination of volatile organic compounds. This method can be used to quantitate most volatile organic compounds including ethylbenzene that have boiling points below 200 deg C and are insoluble or slightly soluble in water.

Under the prescribed conditions for ethylbenzene, the method has a detection limit of 0.06 ug/l, a percent recovery of 99%, and a percent relative standard deviation of 8.6% using a wide bore capillary column; and a detection limit of 0.03 ug/l, a percent recovery of 99%, and a percent relative standard deviation of 5.3% using a narrow bore capillary column.
[USEPA/Office of Solid Waste (OSW); Test Methods for Evaluating Solid Waste, Physical/Chemical Methods SW846 Methods (1986)]**PEER REVIEWED**

OSW Method 8240B. Determination of Volatile Organics Compounds by Gas Chromatography/Mass Spectrometry (GC/MS).
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

OSW Method 5021. Volatile Organic Compounds in Soils and Other Solid Matrices Using Equilibrium Headspace Analysis.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

OSW Method 8020A. Determination of Aromatic Volatile Organics by Gas Chromatography.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

OSW Method 8021A. Analysis of Halogenated and Aromatic Volatiles By Gas Chromatography using Electrolytic Conductivity and Photoionization Detectors in Series: Capillary Column Technique.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

OSW Method 8021A. Halogenated and Aromatic Volatiles By Gas chromatography using Electrolytic Conductivity and Photoionization Detectors in Series: Capillary Technique.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

OSW Method 8240B. Determination of Volatile Organic Compounds by Gas Chromatography/Mass Spectrometry (GC/MS).
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

OSW Method 8260A. Determination of Volatile Organic Compounds by Gas Chromatography/Mass Spectrometry (GC/MS): Capillary Column Technique.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

OSW Method 8260B. Volatile Organic Compounds by Gas Chromatography/Mass Spectrometry (GC/MS): Capillary Column Technique.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

OSW Method 5041. Analysis of Sorbent Cartridges From Volatile Organic Sampling Train by using the Wide-Bore Capillary Column Technique.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

OSW Method 5041A. Protocol for Desorption of Sorbent Cartridges from Volatile Organic Sampling Train (VOST): Wide-Bore Capillary GC/MS Technique.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method OA-002-1. Volatile Organic Compounds by GC/MS Analysis of Tenax/CMS Cartridge and Summa Canister Samples.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VA-001-1. Volatile Organic Compounds (VOCs) in Air Sampled by Sorbent Tubes and Analyzed by Purge and Trap GC.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VA-003-1. Volatile Organic Compounds (VOCs) in Air by Portable GC/PID.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VA-005-1. Volatile Organic Compounds (VOCs) in Ambient Air by Purge and Trap Gas Chromatography.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VA-006-1. Volatile Organic Compounds (VOCs) in Ambient Air by Direct Portable GC/PID.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VA-008-1. Volatile Organic Compounds (VOCs) in Ambient Air by Portable GC/PID with

Direct Sampling via Pump and Sample Loop.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VG-001-1. Volatile Organics in Soil Gas - Adsorbent Tube Method.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VG-006-1. Volatile Organic Compounds (VOCs) in Ambient Air by Purge and Trap GC.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VG-007-1. Halogenated and Aromatic Volatile Organic Compounds (VOCs) in Air and Soil Gas Sampled by Sorbent Tubes and Analyzed by Purge and Trap GC/ELCD/PID.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VG-008-1. Volatile Organic Compounds (VOCs) in Soil Gas sampled by Tenax Tubes and Analyzed by Thermal Desorption GC/PID/ELCD.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VG-010-1. Volatile Organic Compounds (VOCs) in Soil Gas by Direct Portable GC.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VG-011-1. Halogenated and Aromatic Volatile Organic Compounds (VOCs) in Whole Gas Analyzed by Purge and Trap GC/ELCD/PID.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VW-001-1. Volatile Organic Compounds (VOCs) in Water by Purge and Trap GC/PID/ELCD.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VW-002-1. Volatile Organic Compounds (VOCs) in Water by Automated Headspace GC/PID/ELCD.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VW-003-1. Volatile Organic Compounds (VOCs) in Water by Automated Headspace GC/PID/ELCD (Internal Standard).
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VW-004-1. Volatile Organic Compounds (VOCs) in Water by Manual Headspace Portable GC/PID.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VW-008-1. Volatile Organic Compounds (VOCs) in Water by Purge and Trap GC.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VW-010-1. Field Screening for Volatile Organic Compounds (VOCs) in Water and Soil by Headspace GC/PID (Photovac 10S10).
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VW-014-1. Volatile Organic Compounds (VOCs) in Water by Purge and Trap GC/PID/ELCD.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VS-001-1. Volatile Organic Compounds (VOCs) in Soil by Purge and Trap GC/PID/ELC.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VS-002-1. Volatile Organic Compounds (VOCs) in Soil and Sediment by Automated Headspace GC/PID/ELCD.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VW-010-1. Field Screening for Volatile Organic Compounds (VOCs) in Water and Soil by Headspace GC/PID (Photovac 10S10).
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

CLP Method LC_VOA. Analysis of Water for Low concn Volatile Organic Compounds by Gas Chromatography/Mass Spectroscopy.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version

1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

CLP Method MC_VOA. Analysis of Volatile Organics in Multi-Concentration Water Samples by Gas Chromatography with a Mass Spectrometer.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

CLP Method MC_VOA. Analysis of Volatile Organics in Low concn Soil Samples by Gas Chromatography with a Mass Spectrometer.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

CLP Method MC_VOA. Analysis of Volatile Organics in Medium concn Soil Samples by Gas Chromatography with a Mass Spectrometer.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

DOE Method OS040. Rapid Determination Of Volatile Organic Contaminants in Water and Soils by Direct Purge Mass Spectrometry.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

DOE Method OS040. Rapid Determination Of Volatile Organic Contaminants in Water and Soils by Direct Purge Mass Spectrometry.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

DOE Method OS060. Immunoassay for Petroleum Fuel Hydrocarbons in Soil.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

EAD Method 1624. Volatile Organic Compounds by Isotope Dilution GCMS.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

EAD Method 1624. Volatile Organic Compounds by Isotope Dilution GCMS.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

EMSLC Method 502.2. Volatile Organic Compounds in Water by Purge and Trap Capillary Column Gas

Chromatography with Photoionization and Electrolytic Conductivity Detectors in Series.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

EMSLC Method 503.1. Volatile Aromatic and Unsaturated Organic Compounds in Water by Purge and Trap Gas Chromatography.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

EMSLC Method 524.1. Measurement of Purgeable Organic Compounds in Water by Packed Column Gas Chromatography and Mass Spectrometry.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

EMSLC Method 524.2 Measurement of Purgeable Organic Compounds in Water by Capillary Column Gas Chromatography/Mass Spectrometry.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

EMSLC Method 602. Purgeable Aromatics in Wastewater by Gas Chromatography with Photoionization Detection.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

EMSLC Method 624. Protocol for the Analysis of Purgeable Organic Priority Pollutants in Industrial and Municipal Wastewater.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

EMSLC Method 624-S. Analysis of Purgeable Organic Priority Pollutants in Industrial and Municipal Wastewater Treatment Sludge.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

SFSAS Method SFSAS_7. Determination of Purgeable Organics in Sediment.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VS-006-1. Volatile Organic Compounds (VOCs) in Soil and Water by Purge and Trap GC.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER

REVIEWED**

AOB Method VW-011-1. Field Screening for Volatile Organic Compounds (VOCs) in Water and Soil by Purge and Trap GC/PID/ELCD.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

CLP Method OHC. Organics Analysis, Multi-Media, High-Concentration.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

SFSAS Method SFSAS_29. Extraction and Analysis of Organics in Biological Tissue.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

SFSAS Method SFSAS_5. Analysis of Fish for Volatile Organics by Purge and Trap Analysis.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

Sampling Procedures:

AIR SAMPLES WERE COLLECTED IN TEFLON LOOP (3.0 ML).
[IMAMURA K ET AL; BUNSEKI KAGAKU 28 (9): 549 (1979)]**PEER REVIEWED**

NIOSH Method 1501. Analyte: Ethylbenzene. Matrix: Air. Sampler: Solid sorbent tube (coconut shell charcoal, 100 mg/50 mg). Flow Rate: less or equal to 0.2 l/min. Sample Size: 10-24 liters. Shipment: no special specifications. Sample Stability: not determined.
[U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. 1501-1]**PEER REVIEWED**

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[Ogata M, Taguchi T; Int Arch Occup Environ Health 59 (3): 263-72 (1987)]**PEER REVIEWED**

ETHYLBENZENE

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[40 CFR 136 (7/1/91)]**PEER REVIEWED**

EPA Method 1624. Isotope Dilution Purge-and-Trap Gas Chromatography/Mass Spectrometry. This method is applicable for the determination of volatile organic compounds in municpal and industrial discharges. By adding a known amount of a labeled compound to every sample prior to purging, a correction of recovery of the pollutant can be made. If labeled compounds are not available, an internal standard method is used. Under the prescribed conditions, for both the labeled, and unlabeled ethylbenzene the method has a minimum detection level 10 ug/l.The established acceptance performance criteria at 20 ug/l is 9.6 ug/l for the standard deviation of the recovery, with the average recovery of 15.6 to 28.5 ug/l and the labeled cmpd recovery ranging from below detection to 203%.
[40 CFR 136 (7/1/91)]**PEER REVIEWED**

EPA Method 602. Purge-and-Trap Gas Chromatography with photoionization detection for the determination of purgeable aromatics including ethylbenzene in municipal and industrial discharges. Under the prescribed conditionss for ethylbenzene the detection limit is 0.2 ug/l. The method is applicable for use in the concentration range from the method detection limit to times that limit. Precision and method accuracy were found to be directly related to the concentration of the analyte essentially independent of the sample matrix.
[40 CFR 136 (7/1/91)]**PEER REVIEWED**

EPA Method 524.2. Purge-and-Trap Gas Chromatography/Mass Spectrometry for the determination of volatile aromatic compounds in water including finished drinking water, raw source water, and drinking water in any treatment stage. For ethylbenzene the method has a detection limit of 0.06 ug/l and a relative standard deviation of 8.6% with a wide bore capillary column, and a method detection limit of 0.03 ug/l and a relative standard deviation of 5.3% with a narrow bore capillary column.
[USEPA; Methods for the Determinatioon of Organic Compounds in Finished Drinking Water and Raw Source Water (19860]**PEER REVIEWED**

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[USEPA; Methods for the Determination of Organic Compounds in Finished Drinking Water and Raw Source Water (1986)]**PEER REVIEWED**

NIOSH Method 1501. Determination of Aromatic Hydrocarbons by Gas Chromatography with Flame Ionization Detection.
[U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSH Manual of Analytical Methods. 4th ed.Methods A-Z & Supplements. Washington, DC: U.S. Government Printing Office, Aug 1994.]**PEER REVIEWED**

EPA Method 8240. Gas Chromatography/Mass Spectrometry for the determination of volatile organics. This method can be used to quantify most volatile organic compounds including ethylbenzene that have boiling points below 200 deg C and are insoluble or slightly soluble in water. The detection limit is not given. Precision and method accuracy were found to be directly related to the concentration of the analyte and essentially independent of the sample matrix.
[USEPA/Office of Solid Waste (OSW); Test Methods for Evaluating Solid Waste, Physical/Chemical Methods SW846 Methods (1986)]**PEER REVIEWED**

EPA Method 8260. Gas Chromatography/Mass Spectrometry for the determination of volatile organic compounds. This method can be used to quantitate most volatile organic compounds including ethylbenzene that have boiling points below 200 deg C and are insoluble or slightly soluble in water. Under the prescribed conditions for ethylbenzene, the method has a detection limit of 0.06 ug/l, a percent recovery of 99%, and a percent relative standard deviation of 8.6% using a wide bore capillary column; and a detection limit of 0.03 ug/l, a percent recovery of 99%, and a percent relative standard deviation of 5.3% using a narrow bore capillary column.
[USEPA/Office of Solid Waste (OSW); Test Methods for Evaluating Solid Waste, Physical/Chemical Methods SW846 Methods (1986)]**PEER REVIEWED**

OSW Method 8240B. Determination of Volatile Organics Compounds by Gas Chromatography/Mass Spectrometry (GC/MS).
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

OSW Method 5021. Volatile Organic Compounds in Soils and Other Solid Matrices Using Equilibrium Headspace Analysis.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version

1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

OSW Method 8020A. Determination of Aromatic Volatile Organics by Gas Chromatography.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

OSW Method 8021A. Analysis of Halogenated and Aromatic Volatiles By Gas Chromatography using Electrolytic Conductivity and Photoionization Detectors in Series: Capillary Column Technique.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

OSW Method 8021A. Halogenated and Aromatic Volatiles By Gas chromatography using Electrolytic Conductivity and Photoionization Detectors in Series: Capillary Technique.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

OSW Method 8240B. Determination of Volatile Organic Compounds by Gas Chromatography/Mass Spectrometry (GC/MS).
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

OSW Method 8260A. Determination of Volatile Organic Compounds by Gas Chromatography/Mass Spectrometry (GC/MS): Capillary Column Technique.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

OSW Method 8260B. Volatile Organic Compounds by Gas Chromatography/Mass Spectrometry (GC/MS): Capillary Column Technique.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

OSW Method 5041. Analysis of Sorbent Cartridges From Volatile Organic Sampling Train by using the Wide-Bore Capillary Column Technique.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

OSW Method 5041A. Protocol for Desorption of Sorbent Cartridges from Volatile Organic Sampling Train (VOST): Wide-Bore Capillary GC/MS Technique.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method OA-002-1. Volatile Organic Compounds by GC/MS Analysis of Tenax/CMS Cartridge and Summa Canister Samples.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VA-001-1. Volatile Organic Compounds (VOCs) in Air Sampled by Sorbent Tubes and Analyzed by Purge and Trap GC.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VA-003-1. Volatile Organic Compounds (VOCs) in Air by Portable GC/PID.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VA-005-1. Volatile Organic Compounds (VOCs) in Ambient Air by Purge and Trap Gas Chromatography.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VA-006-1. Volatile Organic Compounds (VOCs) in Ambient Air by Direct Portable GC/PID.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VA-008-1. Volatile Organic Compounds (VOCs) in Ambient Air by Portable GC/PID with Direct Sampling via Pump and Sample Loop.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VG-001-1. Volatile Organics in Soil Gas - Adsorbent Tube Method.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VG-006-1. Volatile Organic Compounds (VOCs) in Ambient Air by Purge and Trap GC.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VG-007-1. Halogenated and Aromatic Volatile Organic Compounds (VOCs) in Air and Soil Gas Sampled by Sorbent Tubes and Analyzed by Purge and Trap GC/ELCD/PID.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER

REVIEWED**

AOB Method VG-008-1. Volatile Organic Compounds (VOCs) in Soil Gas sampled by Tenax Tubes and Analyzed by Thermal Desorption GC/PID/ELCD.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VG-010-1. Volatile Organic Compounds (VOCs) in Soil Gas by Direct Portable GC.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VG-011-1. Halogenated and Aromatic Volatile Organic Compounds (VOCs) in Whole Gas Analyzed by Purge and Trap GC/ELCD/PID.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VW-001-1. Volatile Organic Compounds (VOCs) in Water by Purge and Trap GC/PID/ELCD.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VW-002-1. Volatile Organic Compounds (VOCs) in Water by Automated Headspace GC/PID/ELCD.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VW-003-1. Volatile Organic Compounds (VOCs) in Water by Automated Headspace GC/PID/ELCD (Internal Standard).
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VW-004-1. Volatile Organic Compounds (VOCs) in Water by Manual Headspace Portable GC/PID.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VW-008-1. Volatile Organic Compounds (VOCs) in Water by Purge and Trap GC.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VW-010-1. Field Screening for Volatile Organic Compounds (VOCs) in Water and Soil by

Headspace GC/PID (Photovac 10S10).
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VW-014-1. Volatile Organic Compounds (VOCs) in Water by Purge and Trap GC/PID/ELCD.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VS-001-1. Volatile Organic Compounds (VOCs) in Soil by Purge and Trap GC/PID/ELC.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VS-002-1. Volatile Organic Compounds (VOCs) in Soil and Sediment by Automated Headspace GC/PID/ELCD.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VW-010-1. Field Screening for Volatile Organic Compounds (VOCs) in Water and Soil by Headspace GC/PID (Photovac 10S10).
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

CLP Method LC_VOA. Analysis of Water for Low concn Volatile Organic Compounds by Gas Chromatography/Mass Spectroscopy.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

CLP Method MC_VOA. Analysis of Volatile Organics in Multi-Concentration Water Samples by Gas Chromatography with a Mass Spectrometer.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

CLP Method MC_VOA. Analysis of Volatile Organics in Low concn Soil Samples by Gas Chromatography with a Mass Spectrometer.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

CLP Method MC_VOA. Analysis of Volatile Organics in Medium concn Soil Samples by Gas Chromatography with a Mass Spectrometer.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version

1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

DOE Method OS040. Rapid Determination Of Volatile Organic Contaminants in Water and Soils by Direct Purge Mass Spectrometry.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

DOE Method OS040. Rapid Determination Of Volatile Organic Contaminants in Water and Soils by Direct Purge Mass Spectrometry.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

DOE Method OS060. Immunoassay for Petroleum Fuel Hydrocarbons in Soil.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

EAD Method 1624. Volatile Organic Compounds by Isotope Dilution GCMS.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

EAD Method 1624. Volatile Organic Compounds by Isotope Dilution GCMS.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

EMSLC Method 502.2. Volatile Organic Compounds in Water by Purge and Trap Capillary Column Gas Chromatography with Photoionization and Electrolytic Conductivity Detectors in Series.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

EMSLC Method 503.1. Volatile Aromatic and Unsaturated Organic Compounds in Water by Purge and Trap Gas Chromatography.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

EMSLC Method 524.1. Measurement of Purgeable Organic Compounds in Water by Packed Column Gas Chromatography and Mass Spectrometry.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

EMSLC Method 524.2 Measurement of Purgeable Organic Compounds in Water by Capillary Column

Gas Chromatography/Mass Spectrometry.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

EMSLC Method 602. Purgeable Aromatics in Wastewater by Gas Chromatography with Photoionization Detection.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

EMSLC Method 624. Protocol for the Analysis of Purgeable Organic Priority Pollutants in Industrial and Municipal Wastewater.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

EMSLC Method 624-S. Analysis of Purgeable Organic Priority Pollutants in Industrial and Municipal Wastewater Treatment Sludge.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

SFSAS Method SFSAS_7. Determination of Purgeable Organics in Sediment.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VS-006-1. Volatile Organic Compounds (VOCs) in Soil and Water by Purge and Trap GC.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VW-011-1. Field Screening for Volatile Organic Compounds (VOCs) in Water and Soil by Purge and Trap GC/PID/ELCD.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

CLP Method OHC. Organics Analysis, Multi-Media, High-Concentration.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

SFSAS Method SFSAS_29. Extraction and Analysis of Organics in Biological Tissue.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

SFSAS Method SFSAS_5. Analysis of Fish for Volatile Organics by Purge and Trap Analysis. [USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC#4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Sampling Procedures:

AIR SAMPLES WERE COLLECTED IN TEFLON LOOP (3.0 ML).
[IMAMURA K ET AL; BUNSEKI KAGAKU 28 (9): 549 (1979)]**PEER REVIEWED**

NIOSH Method 1501. Analyte: Ethylbenzene. Matrix: Air. Sampler: Solid sorbent tube (coconut shell charcoal, 100 mg/50 mg). Flow Rate: less or equal to 0.2 l/min. Sample Size: 10-24 liters. Shipment: no special specifications. Sample Stability: not determined.
[U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. 1501-1]**PEER REVIEWED**

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Special References:

Special Reports:

HALEY TJ, A REVIEW OF LITERATURE ON ETHYLBENZENE; DANGEROUS PROP IND MATER REP 1(6) 2 (1981). A REVIEW WITH 39 REFERENCES ON CHEMISTRY, METABOLISM, PHARMACOLOGY & TOXICITY OF ETHYLBENZENE.

USEPA; Ambient Water Quality Criteria Document: Ethylbenzene (1980) EPA No. 440/5-8-048.

Environment Canada; Tech Info for Problem Spills: Ethylbenzene (Draft) (1982)

Fishbein L; Ethylbenzene in An Overview of Environmental and Toxicological Aspects of Aromatic Hydrocarbons; Sci Total Environ 44 (3): 269-88 (1985)

Forrest RG et al; Hazardous Mater Spills Conference Proc, Prev, Behav, Control Cleanup Spills Waste Sites (1984) 17-23

Chemical Review: Ethylbenzene; Dangerous Prop Ind Mater Rep 7 (2): 13-35 (1987)

DHHS/ATSDR; Toxicological Profile for Ethylbenzene (1990) ATSDR/TP-90/15

USEPA/ECAO; Ambient Water Quality Criteria Document: Addendum for Ethylbenzene. Final Draft (12/89) ECAO Pub. ECAO-CIN-647

DHHS/NTP; NTP Report on the Toxicity Studies of Ethylbenzene in F344/N Rats and B6C3F1 Mice (Inhalation Studies) NTP Tox 10 (1992)

Toxicology & Carcinogenesis Studies of Ethylbenzene in F344/N Rats and B6C3F1 Mice p.5 Technical Report Series No. 466 (1999) NIH Publication No. 99-3956 U.S. Department of Health and Human Services, National Toxicology Program, National Institute of Environmental Health Sciences, Research Triangle Park, NC 27709

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Special Reports:

HALEY TJ, A REVIEW OF LITERATURE ON ETHYLBENZENE; DANGEROUS PROP IND MATER REP 1(6) 2 (1981). A REVIEW WITH 39 REFERENCES ON CHEMISTRY, METABOLISM, PHARMACOLOGY & TOXICITY OF ETHYLBENZENE.

USEPA; Ambient Water Quality Criteria Document: Ethylbenzene (1980) EPA No. 440/5-8-048.

Environment Canada; Tech Info for Problem Spills: Ethylbenzene (Draft) (1982)

Fishbein L; Ethylbenzene in An Overview of Environmental and Toxicological Aspects of Aromatic Hydrocarbons; Sci Total Environ 44 (3): 269-88 (1985)

Forrest RG et al; Hazardous Mater Spills Conference Proc, Prev, Behav, Control Cleanup Spills Waste Sites (1984) 17-23

Chemical Review: Ethylbenzene; Dangerous Prop Ind Mater Rep 7 (2): 13-35 (1987)

DHHS/ATSDR; Toxicological Profile for Ethylbenzene (1990) ATSDR/TP-90/15

USEPA/ECAO; Ambient Water Quality Criteria Document: Addendum for Ethylbenzene. Final Draft (12/89) ECAO Pub. ECAO-CIN-647

DHHS/NTP; NTP Report on the Toxicity Studies of Ethylbenzene in F344/N Rats and B6C3F1 Mice (Inhalation Studies) NTP Tox 10 (1992)

Toxicology & Carcinogenesis Studies of Ethylbenzene in F344/N Rats and B6C3F1 Mice p.5 Technical Report Series No. 466 (1999) NIH Publication No. 99-3956 U.S. Department of Health and Human Services, National Toxicology Program, National Institute of Environmental Health Sciences, Research Triangle Park, NC 27709

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Synonyms and Identifiers:

Synonyms:

AETHYLBENZOL (GERMAN)
PEER REVIEWED

BENZENE, ETHYL-
PEER REVIEWED

EB
PEER REVIEWED

ETHYLBENZEEN (DUTCH)
PEER REVIEWED

ETHYL BENZENE
PEER REVIEWED

ETHYLBENZOL
PEER REVIEWED

ETILBENZENE (ITALIAN)
PEER REVIEWED

ETYLOBENZEN (POLISH)
PEER REVIEWED

NCI-C56393
PEER REVIEWED

PHENYLETHANE
PEER REVIEWED

Formulations/Preparations:

GRADE: TECHNICAL 99.0%; PURE 99.5%; RESEARCH 99.98%.
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Grade: Technical, pure, research
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 1997. 461]**PEER REVIEWED**

Shipping Name/ Number DOT/UN/NA/IMO:

UN 1175; Ethylbenzene

IMO 3.2; Ethylbenzene

Standard Transportation Number:

49 091 63; Ethylbenzene

EPA Hazardous Waste Number:

F003; A hazardous waste from nonspecific sources when a spent solvent.

RTECS Number:

NIOSH/DA0700000

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Synonyms:

AETHYLBENZOL (GERMAN)
PEER REVIEWED

BENZENE, ETHYL-
PEER REVIEWED

EB
PEER REVIEWED

ETHYLBENZEEN (DUTCH)
PEER REVIEWED

ETHYL BENZENE
PEER REVIEWED

ETHYLBENZOL
PEER REVIEWED

ETILBENZENE (ITALIAN)
PEER REVIEWED

ETYLOBENZEN (POLISH)
PEER REVIEWED

NCI-C56393
PEER REVIEWED

PHENYLETHANE
PEER REVIEWED

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Shipping Name/ Number DOT/UN/NA/IMO:

UN 1175; Ethylbenzene

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ETHYLBENZENE

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For other data, click on the Table of Contents

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For other data, click on the Table of Contents

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F003; A hazardous waste from nonspecific sources when a spent solvent.

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

RTECS Number:

NIOSH/DA0700000

ETHYLBENZENE

CASRN: 100-41-4

For other data, click on the Table of Contents

Administrative Information:

Hazardous Substances Databank Number: 84

Last Revision Date: 20010130

Last Review Date: Reviewed by SRP on 1/29/2000

Update History:

Complete Update on 01/30/2001, 2 fields added/edited/deleted.
Complete Update on 09/12/2000, 1 field added/edited/deleted.
Complete Update on 08/04/2000, 91 fields added/edited/deleted.
Field Update on 02/08/2000, 1 field added/edited/deleted.
Field Update on 02/02/2000, 1 field added/edited/deleted.
Field Update on 11/18/1999, 1 field added/edited/deleted.
Field Update on 09/21/1999, 1 field added/edited/deleted.
Field Update on 08/24/1999, 1 field added/edited/deleted.
Complete Update on 03/29/1999, 3 fields added/edited/deleted.
Field Update on 03/19/1999, 1 field added/edited/deleted.
Field Update on 03/17/1999, 1 field added/edited/deleted.
Complete Update on 02/24/1999, 2 fields added/edited/deleted.
Complete Update on 01/20/1999, 1 field added/edited/deleted.
Complete Update on 11/12/1998, 1 field added/edited/deleted.
Complete Update on 09/03/1998, 1 field added/edited/deleted.
Complete Update on 06/02/1998, 1 field added/edited/deleted.
Complete Update on 02/25/1998, 1 field added/edited/deleted.
Complete Update on 10/17/1997, 1 field added/edited/deleted.
Complete Update on 03/27/1997, 2 fields added/edited/deleted.
Complete Update on 02/26/1997, 1 field added/edited/deleted.
Complete Update on 02/25/1997, 1 field added/edited/deleted.
Complete Update on 10/12/1996, 1 field added/edited/deleted.
Complete Update on 05/14/1996, 1 field added/edited/deleted.
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Complete Update on 04/18/1996, 2 fields added/edited/deleted.
Complete Update on 04/16/1996, 7 fields added/edited/deleted.
Complete Update on 01/18/1996, 1 field added/edited/deleted.
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Complete Update on 05/26/1995, 1 field added/edited/deleted.
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Complete Update on 12/19/1994, 1 field added/edited/deleted.
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Complete Update on 08/24/1994, 1 field added/edited/deleted.

Complete Update on 08/19/1994, 1 field added/edited/deleted.
Complete Update on 07/25/1994, 1 field added/edited/deleted.
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Complete Update on 08/20/1993, 1 field added/edited/deleted.
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Complete Update on 08/07/1993, 1 field added/edited/deleted.
Complete Update on 08/04/1993, 1 field added/edited/deleted.
Complete Update on 04/30/1993, 1 field added/edited/deleted.
Complete Update on 02/05/1993, 1 field added/edited/deleted.
Field update on 12/10/1992, 1 field added/edited/deleted.
Complete Update on 09/14/1992, 72 fields added/edited/deleted.
Field Update on 09/04/1992, 1 field added/edited/deleted.
Field Update on 09/04/1992, 1 field added/edited/deleted.
Complete Update on 08/17/1992, 72 fields added/edited/deleted.
Field Update on 07/29/1992, 1 field added/edited/deleted.
Field Update on 05/29/1992, 1 field added/edited/deleted.
Field Update on 04/16/1992, 1 field added/edited/deleted.
Field Update on 01/13/1992, 1 field added/edited/deleted.
Field Update on 09/12/1991, 1 field added/edited/deleted.
Field Update on 09/10/1991, 1 field added/edited/deleted.
Field Update on 09/10/1991, 1 field added/edited/deleted.
Complete Update on 07/09/1991, 2 fields added/edited/deleted.
Complete Update on 10/10/1990, 1 field added/edited/deleted.
Complete Update on 04/16/1990, 2 fields added/edited/deleted.
Field update on 03/06/1990, 1 field added/edited/deleted.
Complete Update on 01/11/1990, 4 fields added/edited/deleted.
Field Update on 05/05/1989, 1 field added/edited/deleted.
Complete Update on 12/09/1988, 2 fields added/edited/deleted.
Complete Update on 09/23/1988, 1 field added/edited/deleted.
Complete Update on 08/15/1988, 104 fields added/edited/deleted.
Complete Update on 10/03/1986

Record Length: 199409

ETHYLBENZENE

CASRN: 100-41-4

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Hazardous Substances Databank Number: 84

ETHYLBENZENE

CASRN: 100-41-4

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Last Revision Date: 20010130

ETHYLBENZENE

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Last Review Date: Reviewed by SRP on 1/29/2000

ETHYLBENZENE

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Complete Update on 08/07/1993, 1 field added/edited/deleted.
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Field Update on 09/04/1992, 1 field added/edited/deleted.
Complete Update on 08/17/1992, 72 fields added/edited/deleted.
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Field Update on 09/10/1991, 1 field added/edited/deleted.
Complete Update on 07/09/1991, 2 fields added/edited/deleted.
Complete Update on 10/10/1990, 1 field added/edited/deleted.
Complete Update on 04/16/1990, 2 fields added/edited/deleted.
Field update on 03/06/1990, 1 field added/edited/deleted.
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ETHYLBENZENE

CASRN: 100-41-4

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Record Length: 199409

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METHYL ETHYL KETONE

CASRN: 78-93-3

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Best Sections

Synonyms :

ETHYLMETHYLKETON (DUTCH)
PEER REVIEWED

Synonyms :

AETHYLMETHYLKETON (GERMAN)
PEER REVIEWED

Synonyms :

METILETILCHETONE (ITALIAN)
PEER REVIEWED

Synonyms :

METYLOETYLOKETON (POLISH)
PEER REVIEWED

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METHYL ETHYL KETONE

CASRN: 78-93-3

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Human Health Effects:

Evidence for Carcinogenicity:

CLASSIFICATION: D; not classifiable as to human carcinogenicity. BASIS FOR CLASSIFICATION: Based on no human carcinogenicity data and inadequate animal data. HUMAN CARCINOGENICITY DATA: None. ANIMAL CARCINOGENICITY DATA: Inadequate.
[U.S. Environmental Protection Agency's Integrated Risk Information System (IRIS) on methyl ethyl ketone (78-93-3) Available from: http://www.epa.gov/ngispgm3/iris on the Substance File List as of March 15, 2000]**PEER REVIEWED**

Human Toxicity Excerpts:

HIGH ATM CONCN OF **METHYL ETHYL KETONE** IS IRRITATING TO THE EYES, NOSE, AND THROAT AND PROLONGED EXPOSURE MAY PRODUCE CNS DEPRESSION ... NO UNTOWARD EFFECTS HAVE BEEN REPORTED FOR CHRONIC EXPOSURE TO LOW CONCN. PROLONGED SKIN CONTACT MAY DEFAT THE SKIN AND PRODUCE DERMATITIS. IF SPLASHED IN THE EYES IT MAY PRODUCE PAINFUL IRRITATION AND CORNEAL INJURY.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1748]**PEER REVIEWED**

... WORKERS EXPOSED TO 300-500 PPM COMPLAINED OF HEADACHE, IRRITATION, AND NAUSEA. EXPOSURES TO 700 PPM LED TO NO PERMANENT UNTOWARD EFFECTS. MOMENTARY EXPOSURE TO 33,000 AND 100,000 PPM PRODUCED INTOLERABLE IRRITATION OF THE EYES, NOSE, AND THROAT.
[Clayton, G. D. and F. E. Clayton (eds.). Patty's Industrial Hygiene and Toxicology: Volume 2A, 2B, 2C: Toxicology. 3rd ed. New York: John Wiley Sons, 1981-1982. 4730]**PEER REVIEWED**

SHORT EXPOSURE OF WORKERS TO 500 PPM ... IN AIR PROVOKED NAUSEA AND VOMITING ... SEVERAL CASES OF PERIPHERAL NEUROPATHY ... OBSERVED /AFTER/ ACUTE PROLONGED OR REPEATED EXPOSURE. NEUROPATHY IS USUALLY SYMMETRICAL, PAINLESS WITH SENSORY LESIONS PREDOMINATING; IT MAY INVOLVE UPPER OR LOWER LIMBS; IN SOME CASES THE FINGERS HAVE BEEN AFFECTED FOLLOWING IMMERSION ... IN THE LIQUID. DERMATITIS ... REPORTED AFTER IMMERSION IN THE LIQUID AND AFTER EXPOSURE TO CONCN VAPORS. /KETONES/
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 1171]**PEER REVIEWED**

METHYL ETHYL KETONE IS IMPLICATED AS THE CAUSE OF RETROBULBAR NEURITIS IN PT WHO USED THE SOLVENT IN REMOVING PAINT FROM AN AIRPLANE HANGAR.

[BERG EF; ANN OPHTHALMOL 3 (12): 1351 (1971)]**PEER REVIEWED**

Exposure of the forearm for 1 hr/day for 6 consecutive days produced damage to the horny layer of the epithelium. ... **Methyl ethyl ketone** can defat and partially dehydrate the stratum corneum of human skin without producing irritation or inflammation.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1767]**PEER REVIEWED**

A workman splashed his eye accidentally /with **methyl ethyl ketone/,** but the next day had only slight conjunctival hyperemia and no residual corneal injury. Despite the mildness of the injury, in the next few days the affected eye developed severe anterior uveitis triggered by slight trauma.
[Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986. 617]**PEER REVIEWED**

Toxic effects of common organic solvents on workers /were/ examined. The most notable acute effects of occupational exposure to organic solvents are /CNS depression/ and other nerve dysfunctions. The common symptoms of short term exposure are fatigue, headache, nausea, sleep disturbance, and alteration in memory. Psychomotor performance of adverse effects on intellectual or memory functions are demonstrated with psychological test batteries after long-term occupational exposure to organic solvents. The mutagenic, carcinogenic, and toxicological effects of ... **methyl ethyl ketone ...** are summarized. ... In clinical observations, the effects of organic solvents can cause increased excretion of abnormal cells and protein in urine. This indicates the possible correlation between long-term exposure and renal disease.
[Bang KM; Health Hazards in the Occupational Environment 7 (3): 15-29 (1984)]**PEER REVIEWED**

A case of contact urticaria (CU) caused by **methyl ethyl ketone (**MEK) was reported. ... A cotton swab test with MEK to the normal skin on his forearm caused the skin to turn bright red. The spot was itchy, but no induration or edema was noticed. The reaction reached its maximum after 15 minutes and then gradually faded. The test was repeated after two days with the same results. Application of the same grade MEK to five medical staff members produced no reaction. ... MEK should be added to the list of agents that are not only irritants, but can also cause contact urticaria.
[Varigos GA, Nurse DS; Contact Dermatitis 15 (4): 259-60 (1986)]**PEER REVIEWED**

... Has a low toxicity following both acute and chronic exposures.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1748]**PEER REVIEWED**

HIGH ATM CONCN ... ARE IRRITATING TO THE EYES, NOSE, AND THROAT AND PROLONGED EXPOSURE MAY PRODUCE CNS DEPRESSION ... NO UNTOWARD EFFECTS HAVE BEEN REPORTED FOR CHRONIC EXPOSURE TO LOW CONCN. PROLONGED SKIN CONTACT MAY DEFAT THE SKIN AND PRODUCE DERMATITIS. IF SPLASHED IN THE EYES IT MAY PRODUCE PAINFUL IRRITATION AND CORNEAL INJURY.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New

York, NY: John Wiley & Sons Inc., 1993-1994. 1748]**PEER REVIEWED**

To determine whether unchanged solvent urinary concentration could be used as a biological exposure index, workers occupationally exposed to various solvents were studied. Nine unrelated groups (a total of 659 males) working in plastic boat, chemical, plastic button, paint, and shoe factories were studied. Urine samples were collected at the beginning of the workshift and at the end of the first half of the shift. A close relationship (correlation coefficient always above 0.85) between the average environmental solvent concentration (mg/cu m) measured in the breathing zone and the urinary concentration of unchanged solvent (ug/l) was observed.
[Ghittori S et al; Am Ind Hyg Assoc J 48 (9): 786-90 (1987)]**PEER REVIEWED**

... Seventy healthy male and female volunteers, 18 to 32 years old, with no previous prolonged exposure to solvents were exposed to 0 or 250 ppm acetone, 200 ppm MEK, or 125 ppm acetone plus 100 ppm MEK vapors for 4 hours in an exposure chamber. Expired air samples were collected before exposure, after 2 and 4 hours exposure, 90 minutes after exposure ended, and the next morning. Blood samples were collected on the day preceding exposure, at 2 or 4 hours of exposure, 2 hours after exposure ended, and the following day. Samples were analyzed for acetone and MEK by gas or gas/liquid chromatography. ... Blood MEK or acetone concentrations continued to increase throughout exposure, the increases between 2 and 4 hours being larger in the case of acetone. Acetone concentrations in the breath took longer to decrease than those of MEK. No interactive effects were noted in the combined exposures. Blood acetone and MEK concentrations were moderately correlated with their breath concentrations. Blood MEK and acetone concentrations tended to be lower in female subjects than in males; however, the differences were significant only for acetone in the combination exposure after 2 hours exposure and 90 minutes postexposure. ...
[Brown WD et al; The Changing Nature of Work and Workforce, Proceedings of the Third Joint US-Finish Science Symposium p.111-14 (1986)]**PEER REVIEWED**

A 47-yr old woman inadvertently ingested an unknown amt of MEK and was found unconscious, hyperventilating, and suffering from severe metabolic acidosis. Her plasma concn of MEK was 950 mg/L. She responded promptly to an infusion of sodium hydrogen carbonate and was discharged from the hospital after a wk. The metabolic effects of MEK ingestion by humans are not well characterized and it is uncertain that the acidosis was produced by MEK.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.81 (1993)]**PEER REVIEWED**

... exposure to 266-797 mg/cu m (90-270 ppm) for up to 4 hr/day caused his subjects to underestimate times of 5 to 30 sec ... on the other hand, found that a 4-hr exposure of human subjects to 590 mg/cu m (200 ppm) had no significant effect in a variety of behavioral test. These included psychomotor, visual vigilance, dual task, sensorimotor and psychological tests. Solvent mixtures of 295 mg MEK/cu m (100 ppm) and 298 mg acetone/cu m (125 ppm) similarly had no significant effect on the results of these behavioral tests.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.81 (1993)]**PEER REVIEWED**

MEK (0.1 mL) rubbed into volar forearm skin daily for 18 days and left uncovered did not produce

persistent erythema or swelling ... A 5-min contact with 1.5 mL of analytical grade MEK confined to a 20-mm circle on the forearm produced a temporary whitening of the skin, but no visible erythema, alteration in cutaneous blood flow or other indication of irritation to the skin ... .
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.81 (1993)]**PEER REVIEWED**

Long-term exposure of 51 Italian workers to MEK produced indications of neurotoxicity with slightly, but not significantly, reduced nerve conduction velocities and various other symptoms such as headache, loss of appetite and weight, GI upset, dizziness, dermatitis and muscular hypotrophy, but no clinically recognizable neuropathy. ... There has been a brief report of chronic exposure of American workers, in a factory producing coated fabric, to 885-1770 mg MEK/cu m (300-600 ppm) in the apparent absence of other solvents. ... Workers complained of dermatoses and numbness of fingers and arms.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.82 (1993)]**PEER REVIEWED**

In a historical prospective morality study of 446 male workers in two MEK dewaxing plants, with an average follow up of 13.9 years, the observed deaths (46) were below the expected (55.51). There was a slight deficiency of deaths from neoplasms (13 observed; 14.26 expected) but there was a significant incr of deaths from tumors of the buccal cavity and pharynx (2 observed; 0.13 expected). However, there were significantly fewer deaths from lung cancer (1 observed; 6.02 expected). In view of the small numbers, it was concluded that there was no clear evidence of cancer hazard in these workers ... .
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.89 (1993)]**PEER REVIEWED**

The application of MEK to the forearm skin of two volunteers for 1 hr/day on six successive days damaged only the stratum corneum and that the dermal toxicity was similar to ethanol. Opdyke indicated that the application of 20 percent MEK in petrolatum to human forearm skin for 48 hr did not cause any irritation and that no sensitization reactions occurred when the same concentration was tested on 24 volunteers.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1767]**PEER REVIEWED**

Two cases of acute poisoning in a raincoat manufacturing operation where the seams were waterproofed with a resin dissolved in either acetone or MEK were reported. Samples of the workroom air indicated that the MEK concentration ranged from 398 to 561 ppm, whereas the acetone concentration ranged from 330 to 495 ppm. Two female employees were reportedly affected by the solvent vapors on different occasions. The first complained of stomach distress and watery eyes one morning, and later was found unconscious in a rest room. The employee had a strong acetone odor on her breath, but no acetonuria upon admission to the local hospital. She was treated with a CNS stimulant and awoke immediately, but complained of a severe headache. The patient was discharged from the hospital on the day following admission. The second case followed the first one by 1 day and was apparently less severe. The individual fainted and convulsed at the work site but regained consciousness immediately afterwards. At the hospital she was confused and had a headache, but after 1 hr of observation she was allowed to return home.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New

York, NY: John Wiley & Sons Inc., 1993-1994. 1767]**PEER REVIEWED**

A case study where a male patient attempted suicide by ingesting approximately 100 ml of an adhesive cement that contained 39 percent cyclohexanone, 28% MEK, 18% acetone was presented. The individual reportedly drank about 720 ml of sake (10 percent ethanol) 30 min prior to drinking the adhesive solution. The patient was unconscious when taken to a hospital about 2 hr after the ingestion of the solvent mixture. Gastric lavage, plasma exchange, and charcoal hemoperfusion were all performed, and the patient regained consciousness about 7 hr after ingestion; however, signs of systemic toxicity persisted. High blood concentrations of a cyclohexanone metabolite (cyclohexanal) were thought to be responsible for the coma, whereas the hyperglycemia was attributed to acetone.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1767]**PEER REVIEWED**

A case of retrobulbar neuritis in a sailor who was using large quantities of MEK as a paint remover was reported. The affected individual complained of blurred vision, light-headedness, and nausea after being exposed to MEK vapor for 1.5 hr. Upon admission to a military hospital, the patient's near- and far-field visual acuity was reduced and blind spots were markedly enlarged when a white target was viewed. An ophthalmoscopic examination, however, did not reveal any abnormalities. Clinical testing on the day of admission revealed elevations in blood methanol and formaldehyde. Visual acuity returned to normal within 2 days of admission; however, the blood methanol levels did not return to normal until the sixth day of hospitalization. /It was/ concluded that MEK was the causative agent for the optic nerve damage that was observed. The MEK was assumed to have been systemically absorbed both dermally and through the lungs and then partially metabolized to methanol, which subsequently affected the optic nerve and cerebral cortex.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1767]**PEER REVIEWED**

A case of toxic encephalopathy with dementia and cerebellar ataxia in a 38-year-old male who spray-painted a truck in an unventilated garage with a paint that contained toluene, MEK, and propylene glycol. As time passed following the exposure, the individual began to experience memory problems along with headaches, shortness of breath, appetite and sleep disturbances, ataxia, and suicidal depression. Neuropsychological evaluations over a 2.5 year period revealed distinct cognitive, motor, and behavioral changes.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1769]**PEER REVIEWED**

The pharmacokinetics of MEK in 70 male and female volunteers following a 4-hr inhalation exposure either alone (200 ppm) or in combination with acetone (225 ppm, 1:1.25 ratio) was described. Blood and expired air elimination data for the MEK-exposed individuals revealed on average that (1) MEK steady-state breath levels of about 10 to 12 ppm were attained, (2) non-steady-state peak blood levels of 3 to 4 ug/ml occurred, (3) no significant difference in uptake or elimination was observed for males and females, and (4) no appreciable interaction affecting elimination took place with the combined exposures.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and

Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1769]**PEER REVIEWED**

Skin, Eye and Respiratory Irritations:

High atm concn ... are irritating to the eyes, nose, and throat ... .
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1748]**PEER REVIEWED**

Vapor is irritating to human mucous membranes and conjuntivae @ 200 ppm after 15 min ... .
[Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984.,p. II-185]**PEER REVIEWED**

Probable Routes of Human Exposure:

NIOSH has est worker exposure to **methyl ethyl ketone** at 3,031,000 ...
[Sittig, M. Handbook of Toxic and Hazardous Chemicals and Carcinogens, 1985. 2nd ed. Park Ridge, NJ: Noyes Data Corporation, 1985. 601]**PEER REVIEWED**

Artificial leather workers /are at risk of exposure/.
[Arena, J.M. and Drew, R.H. (eds.) Poisoning-Toxicology, Symptoms, Treatments. 5th ed. Springfield, IL: Charles C. Thomas Publisher, 1986. 358]**PEER REVIEWED**

NIOSH (NOES Survey 1981-1983) has statistically estimated that 1,221,857 workers (201,308 of these are female) are potentially exposed to **methyl ethyl ketone** in the US(1). Occupational exposure may be through inhalation and dermal contact with this compound at workplaces where **methyl ethyl ketone** is produced or used(SRC). The 8 hour TWA exposure to **methyl ethyl ketone** was 45.4 ppm in a survey of 50 occupationally exposed male subjects working in a magnetic videotape producing factory(2). These workers had average concns of **methyl ethyl ketone** of 2 ppm and 1.4 mg/l in breath and blood samples respectively(2). The mean concn of **methyl ethyl ketone** in the breathing zones of 47 US plants using polyurethane coatings was 4.33 ppm(3). **Methyl ethyl ketone** was detected in the breathing zones in 20 of 70 samples (mean concn 12 mg/cu m) obtained from autobody shops and spray paint shops in Australia(4).
[(1) NIOSH; National Occupational Exposure Survey (NOES) (1983) (2) Sia Gl et al; Environ Monit Assess 19: 401-11 (1991) (3) Myer HE et al; Am Ind Hyg Assoc J 54: 663-70 (1993) (4) Winder C, Turner PJ; Ann Occup Hyg 36: 385-94 (1992)]**PEER REVIEWED**

The general population may be exposed to **methyl ethyl ketone** through the use of commercially available products containing this compound such as paints, adhesives, and rubber cements(SRC). Exposure will also arise from inhalation of ambient air, ingestion of drinking water and food that contains **methyl ethyl ketone(**SRC). The average blood concn of **methyl ethyl ketone** in 600 non-occupationally exposed individuals in the US was 7.1 ppb(1).
[(1) Ashley DL et al; Clin Chem 40: 1401-04 (1994)]**PEER REVIEWED**

Body Burden:

Detected in 5 of 8 samples of mother's milk from 4 USA urban areas.
[(1) Pellizzari ED et al; Bull Environ Contam Toxicol 28: 322-8 (1982)]**PEER REVIEWED**

The kinetics of inhaled **methyl ethyl ketone (**MEK) in human volunteers was studied in an exposure chamber. Relative pulmonary uptake was about 53% throughout a 4 hr exposure period at 200 ppm. Blood MEK concentration rose steadily until the end of exposure. Repeated bicycle exercise increased the overall blood MEK level markedly in comparison to sedentary activity, with transient peaks in association with cycling; thus blood MEK concentration depended both on the rate of uptake and the amount taken up. Only 3% of the absorbed dose was excreted unchanged by exhalation. A well known metabolite of MEK, 2,3-butanediol, was detected in the urine with maximum rates of excretion at about 6 to 12 hr from the beginning of exposure. About 2% of the MEK dose taken up by the lungs was excreted in the urine as 2,3-butanediol. ... Elimination of MEK in blood appeared to exhibit two phases: the initial alpha-phase (T1/2= 30 min; kel alpha= 0.023) over the first post-exposure hour, followed by the terminal beta-phase (T1/2= 81 min; kel beta= 0.009).
[Liira J et al; Int Arch Occup Environ Health 60 (3): 195-200 (1988)]**PEER REVIEWED**

Worker exposures were investigated in April 1983 at the Hoover Company, North Canton, Ohio. ... Area and personal air samples for numerous contaminants were collected and nonionizing radiation levels were measured. ... General medical questionnaires and blood tests for **methyl ethyl ketone (**MEK) were given to exposed workers. ... No respiratory symptoms or pulmonary function disorders were identified in the foundry workers, and MEK was detected in the blood of only one worker at 1.4 ug/ml. ...
[NIOSH; Health Hazard Evaluation Report No. HETA-82-280-1407 (1984)]**PEER REVIEWED**

METHYL ETHYL KETONE

CASRN: 78-93-3

For other data, click on the Table of Contents

Evidence for Carcinogenicity:

CLASSIFICATION: D; not classifiable as to human carcinogenicity. BASIS FOR CLASSIFICATION: Based on no human carcinogenicity data and inadequate animal data. HUMAN CARCINOGENICITY DATA: None. ANIMAL CARCINOGENICITY DATA: Inadequate.
[U.S. Environmental Protection Agency's Integrated Risk Information System (IRIS) on methyl ethyl ketone (78-93-3) Available from: http://www.epa.gov/ngispgm3/iris on the Substance File List as of March 15, 2000]**PEER REVIEWED**

Select Clear

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2-BUTANONE PEROXIDE

CASRN: 1338-23-4

For other data, click on the Table of Contents

Human Health Effects:

Human Toxicity Excerpts:

CONCN SOLN ARE CORROSIVE TO SKIN & MUCOUS MEMBRANE.
[Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984.,p. II-108]**PEER REVIEWED**

ALL ... /PEROXIDE CATALYSTS/ ARE DANGEROUS TO SKIN & IN PARTICULAR TO MUCOUS MEMBRANE OF EYE ... LIQ PEROXIDES CAN BE ABSORBED BY SKIN, PARTICULARLY **METHYL ETHYL KETONE** PEROXIDE, WHICH CAN CAUSE CERTAIN PHYSIOLOGICAL DISORDERS (HEMOLYTIC ANEMIA).
[Lefaux, R. Practical Toxicology of Plastics. Cleveland: CRC Press Inc., 1968. 145]**PEER REVIEWED**

13 CASES OF ACUTE POISONING WITH KETONOX WERE DESCRIBED. THE EFFECTS OF POISON RESEMBLED THOSE OBSERVED AFTER POISONING WITH LYES OR ACIDS, WITH VOMITING & GASTRIC MUCOSA DAMAGE INCLUDING NECROSIS. THE TOXIC ORAL DOSE WAS BETWEEN 50 & 100 ML.
[WOJDYLA Z ET AL; ARCH MED SADOWEJ KRYMINOL 29 (3): 199-205 (1979)]**PEER REVIEWED**

... Severe eye hazard.
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 1611]**PEER REVIEWED**

- Environmental Fate
- Environmental Abiotic Degradation
- Environmental Bioconcentration
- Soil Adsorption/Mobility
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- Explosive Limits & Potential
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- Hazardous Decomposition

Suicidal ingestion of the peroxide of **methyl ethyl ketone** caused a severe metabolic acidosis, hemolysis, esophageal and gastric necrosis, gastric perforation, and death.
[Ellenhorn, M.J. and D.G. Barceloux. Medical Toxicology - Diagnosis and Treatment of Human Poisoning. New York, NY: Elsevier Science Publishing Co., Inc. 1988. 1000]**PEER REVIEWED**

All 4 peroxides are irritants of the skin and mucous membranes; however, the effects of **methyl ethyl ketone** (MEK, or 2-**butanone**) and cyclohexanone peroxides are much greater than those of benzoyl and dicumyl peroxides. The relevance of studies on hemolytic effects of the peroxides to occupational exposure of man is uncertain, and there are no other conclusive reports of systemic toxic effects.
[Aringer L; Arbetarskyddsstyrelsen, Publikationsservice, 171 84 Solna, Sweden, 64 pp. (1985)]**PEER REVIEWED**

Fatal massive peripheral zonal hepatic necrosis developed in a 47 yr old man who accidentally ingested a solution of **methyl ethyl ketone** peroxide in dimethyl phthalate. Such solutions contain about 10% active oxygen. The clinical course was characterized by temporary cardiac arrest, abdominal burns, severe metabolic acidosis, rapid hepatic failure, rhabdomyolysis and respiratory insufficiency. A fatal outcome resulted 4 days afterwards from hepatic coma associated with blood coagulation disorders. Microscopical examination revealed massive periportal hepatic necrosis accompanied by atypical pseudoductular proliferation. The proliferating cells were probably of bile duct origin and exhibited atypia and mitoses.
[Karhunen PJ et al; Hum Exp Toxicol 9 (3): 197-200 (1990)]**PEER REVIEWED**

This compound ... has a workplace exposure limit of 0.2 ppm (1.5 mg/cu m), which is a ceiling limit and should not be exceeded at any time during the work shift. It is a respiratory tract irritant and a severe eye and skin irritant. The maximum nonirritating strength for skin was 1.5%, for eyes 0.6%. Skin irritation was delayed, with erythema and edema appearing within 2 to 3 days. Eyes washed within 4 sec after exposure resulted in no adverse effects. However, it has been noted that single MEK peroxide exposures to the eye can exacerbate preexisting corneal and limbal disease.
[Clayton, G.D., F.E. Clayton (eds.)

- Protective Equipment & Clothing
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Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 562]**PEER REVIEWED**

Human exposure attests to the corrosive nature of this compound, causing chemical burns of the gastrointestinal tract with residual scarring and stricture of the esophagus. Death 2 to 3 days later was due to hepatic failure after ingestion of this material. An oral dose of 50 to 100 ml is toxic and potentially lethal to adults.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 562]**PEER REVIEWED**

The main toxic effect of most peroxides is irritation of skin, mucous membranes and eyes. Prolonged or intense skin contact or splashes in the eyes may cause severe injury. /Peroxides, Organic and Inorganic/
[International Labour Office. Encyclopaedia of Occupational Health and Safety. 4th edition, Volumes 1-4 1998. Geneva, Switzerland: International Labour Office, 1998.,p. 104.349]**PEER REVIEWED**

Skin, Eye and Respiratory Irritations:

... **Methyl ethyl ketone** peroxide ... /is/ extremely irritating and corrosive to the eyes, with risk of blindness ... .
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 1613]**PEER REVIEWED**

Populations at Special Risk:

Individuals with eye, skin, and chronic respiratory diseases /may be/ at an increased risk. /Hydrogen peroxide/
[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) PublicationNo. 81-123 (3 VOLS).

- [EPA Hazardous Waste Number]
- [RTECS Number]
- [Administrative Information]
- [Hazardous Substances Databank Number]
- [Last Revision Date]
- [Last Review Date]
- [Update History]
- [Record Length]

Washington, DC: U.S. Government Printing Office, Jan. 1981. 1]**PEER REVIEWED**

Probable Routes of Human Exposure:

NIOSH (NOES Survey 1981-1983) has statistically estimated that 16,366 workers are potentially exposed to 2-**butanone** peroxide in the US(1). Analysis of 35 air samples collected in the working environments of 5 Swedish plants manufacturing reinforced plastics detected 2-**butanone** peroxide in 13 samples above the detection limit (0.1 mg/cu m) with a maximum concn of 72 mg/cu m(2). Occupational exposure to 2-**butanone** peroxide may occur through inhalation and dermal contact with this compound at workplaces where 2-**butanone** peroxide is produced or used(SRC). Consumer exposure may occur during the use of fiber glass resin kits for boat and automobile repair(4).

[(1) NIOSH; National Occupational Exposure Survey (NOES) (1983) (2) Bachs A, Runmark S; Inst Vatten-Luftvaardsforsk., Publ. IVL B 836 (1986) (3) Manly, TD; Industrial Chemist 32: 271-6 (1956) (4) Galvin JB, Farr C; Patty's Indust Hyg Toxicol. 4th. Clayton GC, Clayton FE, eds. NY, NY: Wiley IIA: 562 (1993)]**PEER REVIEWED**

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HSDB Search Results

for METHYL ETHYL KETONE 78-93-3

Information added from CHEMID:
Chemid Name: **methylethyl ketone [78-93-3]**
(butanone, metyloetyloketon, metiletilchetone, methyl acetone, meetco, ethylmethylketon, aethylmethylketon)
methyl ethyl ketone Chemid Name: **methylethyl ketone [78-93-3]**
(butanone, metyloetyloketon, metiletilchetone, methyl acetone, meetco, ethylmethylketon, aethylmethylketon)

Query:

Registry Numbers:
78-93-3 78-93-3
~
1 record contains the exact substance name or CAS registry number.
139 records contain all of the query terms anywhere in the record.

Items **1** through **20** of **140** **Pages:** 1 2 3 4 5 6 7

*Substance Names are sorted in **relevancy ranked** order.*

Substance Name

The following is the primary record for the chemical. All of the query terms were found.

1 **METHYL ETHYL KETONE**
78-93-3

The following 139 records contain one or more of the requested chemical name(s) and all of the query terms anywhere in the record.

2 **2-BUTANONE PEROXIDE**
1338-23-4

3 **N-NITROSONORNICOTINE**
16543-55-8

4 **3,3-DIMETHYL-2-BUTANONE**
75-97-8

5 **THIOFANOX**
39196-18-4

6 **TRIADIMEFON**
43121-43-3

7 **VITAMIN A**
68-26-8

8 **ACETOIN**
513-86-0

9 **ETHANOL**
64-17-5

10 **SEC-BUTYL ALCOHOL**
78-92-2

11 **3-XYLENE**
108-38-3

12 **2-HEXANONE**
591-78-6

13 **DIACETYL**
431-03-8

14 **N-NITROSOPYRROLIDINE**
930-55-2

15 **METHYL ISOBUTYL KETONE**
108-10-1

16 **3-HEPTANONE**
106-35-4

17 **CAPSAICIN**
404-86-4

18 **METHYL ISOPROPENYL KETONE**
814-78-8

19 **ACETONE**
67-64-1

20 **3-PENTANONE**
96-22-0

Items **1** through **20** of **140** **Pages:** 1 2 3 4 5 6 7

METHYL ETHYL KETONE

CASRN: 78-93-3

For other data, click on the Table of Contents

Synonyms:

ETHYLMETHYLKETON (DUTCH)

PEER REVIEWED

METHYL ETHYL KETONE

CASRN: 78-93-3

For other data, click on the Table of Contents

Synonyms:

AETHYLMETHYLKETON (GERMAN)

PEER REVIEWED

METHYL ETHYL KETONE

CASRN: 78-93-3

For other data, click on the Table of Contents

Synonyms:

METILETILCHETONE (ITALIAN)

PEER REVIEWED

METHYL ETHYL KETONE

CASRN: 78-93-3

For other data, click on the Table of Contents

Synonyms:

METYLOETYLOKETON (POLISH)

PEER REVIEWED

METHYL ETHYL KETONE

CASRN: 78-93-3

For other data, click on the Table of Contents

Human Health Effects:

Evidence for Carcinogenicity:

CLASSIFICATION: D; not classifiable as to human carcinogenicity. BASIS FOR CLASSIFICATION: Based on no human carcinogenicity data and inadequate animal data. HUMAN CARCINOGENICITY DATA: None. ANIMAL CARCINOGENICITY DATA: Inadequate.
[U.S. Environmental Protection Agency's Integrated Risk Information System (IRIS) on methyl ethyl ketone (78-93-3) Available from: http://www.epa.gov/ngispgm3/iris on the Substance File List as of March 15, 2000]**PEER REVIEWED**

Human Toxicity Excerpts:

HIGH ATM CONCN OF **METHYL ETHYL KETONE** IS IRRITATING TO THE EYES, NOSE, AND THROAT AND PROLONGED EXPOSURE MAY PRODUCE CNS DEPRESSION ... NO UNTOWARD EFFECTS HAVE BEEN REPORTED FOR CHRONIC EXPOSURE TO LOW CONCN. PROLONGED SKIN CONTACT MAY DEFAT THE SKIN AND PRODUCE DERMATITIS. IF SPLASHED IN THE EYES IT MAY PRODUCE PAINFUL IRRITATION AND CORNEAL INJURY.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1748]**PEER REVIEWED**

... WORKERS EXPOSED TO 300-500 PPM COMPLAINED OF HEADACHE, IRRITATION, AND NAUSEA. EXPOSURES TO 700 PPM LED TO NO PERMANENT UNTOWARD EFFECTS. MOMENTARY EXPOSURE TO 33,000 AND 100,000 PPM PRODUCED INTOLERABLE IRRITATION OF THE EYES, NOSE, AND THROAT.
[Clayton, G. D. and F. E. Clayton (eds.). Patty's Industrial Hygiene and Toxicology: Volume 2A, 2B, 2C: Toxicology. 3rd ed. New York: John Wiley Sons, 1981-1982. 4730]**PEER REVIEWED**

SHORT EXPOSURE OF WORKERS TO 500 PPM ... IN AIR PROVOKED NAUSEA AND VOMITING ... SEVERAL CASES OF PERIPHERAL NEUROPATHY ... OBSERVED /AFTER/ ACUTE PROLONGED OR REPEATED EXPOSURE. NEUROPATHY IS USUALLY SYMMETRICAL, PAINLESS WITH SENSORY LESIONS PREDOMINATING; IT MAY INVOLVE UPPER OR LOWER LIMBS; IN SOME CASES THE FINGERS HAVE BEEN AFFECTED FOLLOWING IMMERSION ... IN THE LIQUID. DERMATITIS ... REPORTED AFTER IMMERSION IN THE LIQUID AND AFTER EXPOSURE TO CONCN VAPORS. /KETONES/
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 1171]**PEER REVIEWED**

METHYL ETHYL KETONE IS IMPLICATED AS THE CAUSE OF RETROBULBAR NEURITIS IN PT WHO USED THE SOLVENT IN REMOVING PAINT FROM AN AIRPLANE HANGAR.

[BERG EF; ANN OPHTHALMOL 3 (12): 1351 (1971)]**PEER REVIEWED**

Exposure of the forearm for 1 hr/day for 6 consecutive days produced damage to the horny layer of the epithelium. ... **Methyl ethyl ketone** can defat and partially dehydrate the stratum corneum of human skin without producing irritation or inflammation.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1767]**PEER REVIEWED**

A workman splashed his eye accidentally /with **methyl ethyl ketone/,** but the next day had only slight conjunctival hyperemia and no residual corneal injury. Despite the mildness of the injury, in the next few days the affected eye developed severe anterior uveitis triggered by slight trauma.
[Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986. 617]**PEER REVIEWED**

Toxic effects of common organic solvents on workers /were/ examined. The most notable acute effects of occupational exposure to organic solvents are /CNS depression/ and other nerve dysfunctions. The common symptoms of short term exposure are fatigue, headache, nausea, sleep disturbance, and alteration in memory. Psychomotor performance of adverse effects on intellectual or memory functions are demonstrated with psychological test batteries after long-term occupational exposure to organic solvents. The mutagenic, carcinogenic, and toxicological effects of ... **methyl ethyl ketone ...** are summarized. ... In clinical observations, the effects of organic solvents can cause increased excretion of abnormal cells and protein in urine. This indicates the possible correlation between long-term exposure and renal disease.
[Bang KM; Health Hazards in the Occupational Environment 7 (3): 15-29 (1984)]**PEER REVIEWED**

A case of contact urticaria (CU) caused by **methyl ethyl ketone (**MEK) was reported. ... A cotton swab test with MEK to the normal skin on his forearm caused the skin to turn bright red. The spot was itchy, but no induration or edema was noticed. The reaction reached its maximum after 15 minutes and then gradually faded. The test was repeated after two days with the same results. Application of the same grade MEK to five medical staff members produced no reaction. ... MEK should be added to the list of agents that are not only irritants, but can also cause contact urticaria.
[Varigos GA, Nurse DS; Contact Dermatitis 15 (4): 259-60 (1986)]**PEER REVIEWED**

... Has a low toxicity following both acute and chronic exposures.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1748]**PEER REVIEWED**

HIGH ATM CONCN ... ARE IRRITATING TO THE EYES, NOSE, AND THROAT AND PROLONGED EXPOSURE MAY PRODUCE CNS DEPRESSION ... NO UNTOWARD EFFECTS HAVE BEEN REPORTED FOR CHRONIC EXPOSURE TO LOW CONCN. PROLONGED SKIN CONTACT MAY DEFAT THE SKIN AND PRODUCE DERMATITIS. IF SPLASHED IN THE EYES IT MAY PRODUCE PAINFUL IRRITATION AND CORNEAL INJURY.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New

York, NY: John Wiley & Sons Inc., 1993-1994. 1748]**PEER REVIEWED**

To determine whether unchanged solvent urinary concentration could be used as a biological exposure index, workers occupationally exposed to various solvents were studied. Nine unrelated groups (a total of 659 males) working in plastic boat, chemical, plastic button, paint, and shoe factories were studied. Urine samples were collected at the beginning of the workshift and at the end of the first half of the shift. A close relationship (correlation coefficient always above 0.85) between the average environmental solvent concentration (mg/cu m) measured in the breathing zone and the urinary concentration of unchanged solvent (ug/l) was observed.
[Ghittori S et al; Am Ind Hyg Assoc J 48 (9): 786-90 (1987)]**PEER REVIEWED**

... Seventy healthy male and female volunteers, 18 to 32 years old, with no previous prolonged exposure to solvents were exposed to 0 or 250 ppm acetone, 200 ppm MEK, or 125 ppm acetone plus 100 ppm MEK vapors for 4 hours in an exposure chamber. Expired air samples were collected before exposure, after 2 and 4 hours exposure, 90 minutes after exposure ended, and the next morning. Blood samples were collected on the day preceding exposure, at 2 or 4 hours of exposure, 2 hours after exposure ended, and the following day. Samples were analyzed for acetone and MEK by gas or gas/liquid chromatography. ... Blood MEK or acetone concentrations continued to increase throughout exposure, the increases between 2 and 4 hours being larger in the case of acetone. Acetone concentrations in the breath took longer to decrease than those of MEK. No interactive effects were noted in the combined exposures. Blood acetone and MEK concentrations were moderately correlated with their breath concentrations. Blood MEK and acetone concentrations tended to be lower in female subjects than in males; however, the differences were significant only for acetone in the combination exposure after 2 hours exposure and 90 minutes postexposure. ...
[Brown WD et al; The Changing Nature of Work and Workforce, Proceedings of the Third Joint US-Finish Science Symposium p.111-14 (1986)]**PEER REVIEWED**

A 47-yr old woman inadvertently ingested an unknown amt of MEK and was found unconscious, hyperventilating, and suffering from severe metabolic acidosis. Her plasma concn of MEK was 950 mg/L. She responded promptly to an infusion of sodium hydrogen carbonate and was discharged from the hospital after a wk. The metabolic effects of MEK ingestion by humans are not well characterized and it is uncertain that the acidosis was produced by MEK.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.81 (1993)]**PEER REVIEWED**

... exposure to 266-797 mg/cu m (90-270 ppm) for up to 4 hr/day caused his subjects to underestimate times of 5 to 30 sec ... on the other hand, found that a 4-hr exposure of human subjects to 590 mg/cu m (200 ppm) had no significant effect in a variety of behavioral test. These included psychomotor, visual vigilance, dual task, sensorimotor and psychological tests. Solvent mixtures of 295 mg MEK/cu m (100 ppm) and 298 mg acetone/cu m (125 ppm) similarly had no significant effect on the results of these behavioral tests.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.81 (1993)]**PEER REVIEWED**

MEK (0.1 mL) rubbed into volar forearm skin daily for 18 days and left uncovered did not produce

persistent erythema or swelling ... A 5-min contact with 1.5 mL of analytical grade MEK confined to a 20-mm circle on the forearm produced a temporary whitening of the skin, but no visible erythema, alteration in cutaneous blood flow or other indication of irritation to the skin ... .
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.81 (1993)]**PEER REVIEWED**

Long-term exposure of 51 Italian workers to MEK produced indications of neurotoxicity with slightly, but not significantly, reduced nerve conduction velocities and various other symptoms such as headache, loss of appetite and weight, GI upset, dizziness, dermatitis and muscular hypotrophy, but no clinically recognizable neuropathy. ... There has been a brief report of chronic exposure of American workers, in a factory producing coated fabric, to 885-1770 mg MEK/cu m (300-600 ppm) in the apparent absence of other solvents. ... Workers complained of dermatoses and numbness of fingers and arms.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.82 (1993)]**PEER REVIEWED**

In a historical prospective morality study of 446 male workers in two MEK dewaxing plants, with an average follow up of 13.9 years, the observed deaths (46) were below the expected (55.51). There was a slight deficiency of deaths from neoplasms (13 observed; 14.26 expected) but there was a significant incr of deaths from tumors of the buccal cavity and pharynx (2 observed; 0.13 expected). However, there were significantly fewer deaths from lung cancer (1 observed; 6.02 expected). In view of the small numbers, it was concluded that there was no clear evidence of cancer hazard in these workers ... .
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.89 (1993)]**PEER REVIEWED**

The application of MEK to the forearm skin of two volunteers for 1 hr/day on six successive days damaged only the stratum corneum and that the dermal toxicity was similar to ethanol. Opdyke indicated that the application of 20 percent MEK in petrolatum to human forearm skin for 48 hr did not cause any irritation and that no sensitization reactions occurred when the same concentration was tested on 24 volunteers.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1767]**PEER REVIEWED**

Two cases of acute poisoning in a raincoat manufacturing operation where the seams were waterproofed with a resin dissolved in either acetone or MEK were reported. Samples of the workroom air indicated that the MEK concentration ranged from 398 to 561 ppm, whereas the acetone concentration ranged from 330 to 495 ppm. Two female employees were reportedly affected by the solvent vapors on different occasions. The first complained of stomach distress and watery eyes one morning, and later was found unconscious in a rest room. The employee had a strong acetone odor on her breath, but no acetonuria upon admission to the local hospital. She was treated with a CNS stimulant and awoke immediately, but complained of a severe headache. The patient was discharged from the hospital on the day following admission. The second case followed the first one by 1 day and was apparently less severe. The individual fainted and convulsed at the work site but regained consciousness immediately afterwards. At the hospital she was confused and had a headache, but after 1 hr of observation she was allowed to return home.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New

York, NY: John Wiley & Sons Inc., 1993-1994. 1767]**PEER REVIEWED**

A case study where a male patient attempted suicide by ingesting approximately 100 ml of an adhesive cement that contained 39 percent cyclohexanone, 28% MEK, 18% acetone was presented. The individual reportedly drank about 720 ml of sake (10 percent ethanol) 30 min prior to drinking the adhesive solution. The patient was unconscious when taken to a hospital about 2 hr after the ingestion of the solvent mixture. Gastric lavage, plasma exchange, and charcoal hemoperfusion were all performed, and the patient regained consciousness about 7 hr after ingestion; however, signs of systemic toxicity persisted. High blood concentrations of a cyclohexanone metabolite (cyclohexanal) were thought to be responsible for the coma, whereas the hyperglycemia was attributed to acetone.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1767]**PEER REVIEWED**

A case of retrobulbar neuritis in a sailor who was using large quantities of MEK as a paint remover was reported. The affected individual complained of blurred vision, light-headedness, and nausea after being exposed to MEK vapor for 1.5 hr. Upon admission to a military hospital, the patient's near- and far-field visual acuity was reduced and blind spots were markedly enlarged when a white target was viewed. An ophthalmoscopic examination, however, did not reveal any abnormalities. Clinical testing on the day of admission revealed elevations in blood methanol and formaldehyde. Visual acuity returned to normal within 2 days of admission; however, the blood methanol levels did not return to normal until the sixth day of hospitalization. /It was/ concluded that MEK was the causative agent for the optic nerve damage that was observed. The MEK was assumed to have been systemically absorbed both dermally and through the lungs and then partially metabolized to methanol, which subsequently affected the optic nerve and cerebral cortex.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1767]**PEER REVIEWED**

A case of toxic encephalopathy with dementia and cerebellar ataxia in a 38-year-old male who spray-painted a truck in an unventilated garage with a paint that contained toluene, MEK, and propylene glycol. As time passed following the exposure, the individual began to experience memory problems along with headaches, shortness of breath, appetite and sleep disturbances, ataxia, and suicidal depression. Neuropsychological evaluations over a 2.5 year period revealed distinct cognitive, motor, and behavioral changes.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1769]**PEER REVIEWED**

The pharmacokinetics of MEK in 70 male and female volunteers following a 4-hr inhalation exposure either alone (200 ppm) or in combination with acetone (225 ppm, 1:1.25 ratio) was described. Blood and expired air elimination data for the MEK-exposed individuals revealed on average that (1) MEK steady-state breath levels of about 10 to 12 ppm were attained, (2) non-steady-state peak blood levels of 3 to 4 ug/ml occurred, (3) no significant difference in uptake or elimination was observed for males and females, and (4) no appreciable interaction affecting elimination took place with the combined exposures.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and

Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1769]**PEER REVIEWED**

Skin, Eye and Respiratory Irritations:

High atm concn ... are irritating to the eyes, nose, and throat ... .
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1748]**PEER REVIEWED**

Vapor is irritating to human mucous membranes and conjuntivae @ 200 ppm after 15 min ... .
[Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984.,p. II-185]**PEER REVIEWED**

Probable Routes of Human Exposure:

NIOSH has est worker exposure to **methyl ethyl ketone** at 3,031,000 ...
[Sittig, M. Handbook of Toxic and Hazardous Chemicals and Carcinogens, 1985. 2nd ed. Park Ridge, NJ: Noyes Data Corporation, 1985. 601]**PEER REVIEWED**

Artificial leather workers /are at risk of exposure/.
[Arena, J.M. and Drew, R.H. (eds.) Poisoning-Toxicology, Symptoms, Treatments. 5th ed. Springfield, IL: Charles C. Thomas Publisher, 1986. 358]**PEER REVIEWED**

NIOSH (NOES Survey 1981-1983) has statistically estimated that 1,221,857 workers (201,308 of these are female) are potentially exposed to **methyl ethyl ketone** in the US(1). Occupational exposure may be through inhalation and dermal contact with this compound at workplaces where **methyl ethyl ketone** is produced or used(SRC). The 8 hour TWA exposure to **methyl ethyl ketone** was 45.4 ppm in a survey of 50 occupationally exposed male subjects working in a magnetic videotape producing factory(2). These workers had average concns of **methyl ethyl ketone** of 2 ppm and 1.4 mg/l in breath and blood samples respectively(2). The mean concn of **methyl ethyl ketone** in the breathing zones of 47 US plants using polyurethane coatings was 4.33 ppm(3). **Methyl ethyl ketone** was detected in the breathing zones in 20 of 70 samples (mean concn 12 mg/cu m) obtained from autobody shops and spray paint shops in Australia(4).
[(1) NIOSH; National Occupational Exposure Survey (NOES) (1983) (2) Sia Gl et al; Environ Monit Assess 19: 401-11 (1991) (3) Myer HE et al; Am Ind Hyg Assoc J 54: 663-70 (1993) (4) Winder C, Turner PJ; Ann Occup Hyg 36: 385-94 (1992)]**PEER REVIEWED**

The general population may be exposed to **methyl ethyl ketone** through the use of commercially available products containing this compound such as paints, adhesives, and rubber cements(SRC). Exposure will also arise from inhalation of ambient air, ingestion of drinking water and food that contains **methyl ethyl ketone(**SRC). The average blood concn of **methyl ethyl ketone** in 600 non-occupationally exposed individuals in the US was 7.1 ppb(1).
[(1) Ashley DL et al; Clin Chem 40: 1401-04 (1994)]**PEER REVIEWED**

Body Burden:

Detected in 5 of 8 samples of mother's milk from 4 USA urban areas.
[(1) Pellizzari ED et al; Bull Environ Contam Toxicol 28: 322-8 (1982)]**PEER REVIEWED**

The kinetics of inhaled **methyl ethyl ketone (**MEK) in human volunteers was studied in an exposure chamber. Relative pulmonary uptake was about 53% throughout a 4 hr exposure period at 200 ppm. Blood MEK concentration rose steadily until the end of exposure. Repeated bicycle exercise increased the overall blood MEK level markedly in comparison to sedentary activity, with transient peaks in association with cycling; thus blood MEK concentration depended both on the rate of uptake and the amount taken up. Only 3% of the absorbed dose was excreted unchanged by exhalation. A well known metabolite of MEK, 2,3-butanediol, was detected in the urine with maximum rates of excretion at about 6 to 12 hr from the beginning of exposure. About 2% of the MEK dose taken up by the lungs was excreted in the urine as 2,3-butanediol. ... Elimination of MEK in blood appeared to exhibit two phases: the initial alpha-phase (T1/2= 30 min; kel alpha= 0.023) over the first post-exposure hour, followed by the terminal beta-phase (T1/2= 81 min; kel beta= 0.009).
[Liira J et al; Int Arch Occup Environ Health 60 (3): 195-200 (1988)]**PEER REVIEWED**

Worker exposures were investigated in April 1983 at the Hoover Company, North Canton, Ohio. ... Area and personal air samples for numerous contaminants were collected and nonionizing radiation levels were measured. ... General medical questionnaires and blood tests for **methyl ethyl ketone (**MEK) were given to exposed workers. ... No respiratory symptoms or pulmonary function disorders were identified in the foundry workers, and MEK was detected in the blood of only one worker at 1.4 ug/ml. ...
[NIOSH; Health Hazard Evaluation Report No. HETA-82-280-1407 (1984)]**PEER REVIEWED**

Emergency Medical Treatment:

Emergency Medical Treatment:

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The following Overview, *** KETONES ***, is relevant for this HSDB record chemical.

Life Support:

- This overview assumes that basic life support measures have been instituted.

Clinical Effects:

SUMMARY OF EXPOSURE

0.2.1.1 ACUTE EXPOSURE

- ACUTE EXPOSURE (ORAL) - Most available information concerns inhalational or dermal exposure. A few cases involving ingestion of **methyl ethyl ketone (**and co-ingestants) or ketone peroxide (with co-ingestants) have resulted in CNS depression, respiratory depression or corrosive effects and sequelae.
- ACUTE INHALATION - The effects vary, depending on extent and duration of exposure. Eye, nose and throat irritation, nausea, headache, vertigo, incoordination, CNS depression, narcosis and cardiorespiratory failure can occur. In most cases, recovery is usually rapid and complete.
- CHRONIC EXPOSURE - The major concern with chronic exposure is axonal neuropathy with secondary myelin damage; usually manifested as paresthesias and muscle weakness. Only six-carbon, linear chain ketones metabolized to gamma-diketones (such as methyl n-butyl ketone) are implicated.
- EYE EXPOSURE - Splash contact causes irritation, which may be slight, moderate, or severe, depending on the ketone. Vapors can cause irritation and lacrimation.
- ROUTES OF EXPOSURE - Ketones are absorbed by ingestion, inhalation, and dermal exposure.
- RELATED COMPOUNDS - Exposure to ketone solvents (**methyl ethyl ketone,** methyl isobutyl ketone, etc) must be distinguished from exposure to the peroxides of these same ketones. KETONE PEROXIDES are highly reactive and corrosive. Management of ketone peroxide exposure is discussed in a separate document.

HEENT

0.2.4.1 ACUTE EXPOSURE

- Splash contact causes irritation, which may be slight, moderate, or severe, depending on the specific ketone; vapors may cause irritation and lacrimation.

CARDIOVASCULAR

0.2.5.1 ACUTE EXPOSURE

- Tachycardia may occur.

RESPIRATORY

0.2.6.1 ACUTE EXPOSURE

- Ingestion of significant amounts may cause respiratory depression. Inhalation exposure may produce an anesthetic type of respiratory depression, dyspnea, and

gasping. Pulmonary aspiration may result in chemical pneumonitis.

NEUROLOGIC

0.2.7.1 ACUTE EXPOSURE

- Acute inhalation exposure causes a progression of CNS effects, from headache, vertigo, incoordination, narcosis, dizziness, and tremor, to coma. Peripheral neuropathy has been reported following exposure to methyl-n-butyl ketone and 2,5-hexanedione. Trimethylnonanone is not associated with narcosis.
- Chronic exposure causes axonal neuropathy with secondary myelin damage, usually manifested as paresthesias and muscle weakness. Only six-carbon, linear chain ketones metabolized to gamma-diketones (such as methyl n-butyl ketone) are implicated.

GASTROINTESTINAL

0.2.8.1 ACUTE EXPOSURE

- Nausea and vomiting may occur.

HEPATIC

0.2.9.1 ACUTE EXPOSURE

- Ketones may potentiate the hepatotoxicity of halogenated hydrocarbons. They may also inhibit aromatic hydrocarbon metabolism.

ACID-BASE

0.2.11.1 ACUTE EXPOSURE

- Metabolic acidosis has been reported.

DERMATOLOGIC

0.2.14.1 ACUTE EXPOSURE

- Skin exposure to the liquid or vapor may result in dermatitis and paresthesias of affected areas. Contact urticaria has also been reported.

REPRODUCTIVE HAZARDS

- Limited studies have generally documented little or no effect of ketones on reproduction in experimental animals. Human data is lacking. 2,5-Hexanedione has an effect on spermatogenesis in male experimental animals.

CARCINOGENICITY

0.2.21.1 IARC CATEGORY

- The ketones are generally unclassified by IARC. Those agents evaluated by IARC have been classified as having insufficient evidence to determine human carcinogenicity.

0.2.21.2 HUMAN OVERVIEW

- No adequate human studies exist for the agents in this category.

0.2.21.3 ANIMAL OVERVIEW

- Experimental animal studies are limited, but are generally negative, and agents in this group have little mutagenic activity.

GENOTOXICITY

- Extremely limited data is available for this class of agents. For many specific ketones, no data is available. Some studies report positive findings, but this category of agents appears to be generally non-mutagenic or only weakly mutagenic.

Laboratory:

- Plasma ketone levels are not clinically useful.
- If pulmonary aspiration is suspected, monitor chest x-ray and arterial blood gases or pulse oximetry.

Treatment Overview:

ORAL EXPOSURE

- With ingestion of small amounts the major concern is pulmonary aspiration and gastrointestinal decontamination is not recommended. With ingestion of large amounts there is potential for systemic toxicity from gastrointestinal absorption and GI decontamination is suggested, keeping in mind that pulmonary aspiration is still a concern.
- If the patient is obtunded, seizing, or has significant alterations in mental status, a cuffed endotracheal tube should be inserted prior to gastric aspiration.

1. For moderate ingestions (less than 100 milliliters) activated charcoal alone is recommended.
2. For large ingestions that have occurred within the past hour, careful gastric aspiration followed by activated charcoal is recommended.
   a. The lavage tube should be flexible, well lubricated with a water soluble gel to minimize gagging and vomiting, and of a large enough diameter to minimize vomiting of gastric contents around the tube and potential pulmonary aspiration.
   b. After the tube is in place, evacuate gastric contents rapidly. Repeated instillation of fluid to wash out the stomach is NOT suggested as it probably does not significantly enhance the removal of liquids and may enhance the potential for pulmonary aspiration.
   c. Instill activated charcoal prior to withdrawing the tube.
   d. For ingestions that have occurred more than 2 hours

ago, gastric decontamination is not likely to be of benefit and is generally not warranted.

- Administer activated charcoal for moderate or large ingestions.

1. ACTIVATED CHARCOAL: Administer charcoal as slurry (240 mL water/30 g charcoal). Usual dose: 25 to 100 g in adults/adolescents, 25 to 50 g in children (1 to 12 years), and 1 g/kg in infants less than 1 year old.

- ACIDOSIS - Correct severe acidosis (pH < 7.1) with intravenous sodium bicarbonate. About 1 to 2 milliequivalents/kilogram is a useful starting dose. Monitor arterial blood gases to guide bicarbonate therapy.

INHALATION EXPOSURE

- DECONTAMINATION: Move patient to fresh air. Monitor for respiratory distress. If cough or difficulty in breathing develops, evaluate for respiratory tract irritation, bronchitis, or pneumonitis. Administer 100 percent humidified supplemental oxygen with assisted ventilation as required.

EYE EXPOSURE

- DECONTAMINATION: Exposed eyes should be irrigated with copious amounts of tepid water for at least 15 minutes. If irritation, pain, swelling, lacrimation, or photophobia persist, the patient should be seen in a health care facility.

DERMAL EXPOSURE

- DECONTAMINATION: Wash exposed area extremely thoroughly with soap and water. A physician may need to examine the area if irritation or pain persists.
- Treat dermal irritation or burns with standard topical therapy. Patients developing dermal hypersensitivity reactions may require treatment with systemic or topical corticosteroids or antihistamines.

Range of Toxicity:

- The minimal toxic or lethal dose is variable and not well defined. Toxic effects following inhalation exposure depend on air concentration, time of exposure and underlying diseases.
- Exposure to airborne concentrations greater than 300 ppm of **methyl ethyl ketone** may result in discomfort and CNS depression. Methyl-isobutyl ketone produces irritation at an airborne concentration of 100 ppm (Hjelm et al, 1990).

[Rumack BH: POISINDEX(R) Information System. Micromedex, Inc., Englewood, CO, 2001; CCIS Volume 107, edition exp February, 2001. Hall AH & Rumack BH (Eds):TOMES(R) Information System. Micromedex, Inc., Englewood, CO, 2001; CCIS Volume 107, edition exp February, 2001.] **PEER REVIEWED**

Antidote and Emergency Treatment:

For immediate first aid: Ensure that adequate decontamination has been carried out. If victim is not breathing, start artificial respiration, preferably with a demand-valve resuscitator, bag-valve-mask device, or pocket mask as trained. Perform CPR if necessary. Immediately flush contaminated eyes with gently flowing water. Do not induce vomiting. If vomiting occurs, lean patient forward or place on left side (head-down position, if possible) to maintain an open airway and prevent aspiration. Keep victim quiet and maintain normal body temperature. Obtain medical attention. /Ketones and related compounds/
[Bronstein, A.C., P.L. Currance; Emergency Care for Hazardous Materials Exposure. 2nd ed. St. Louis, MO. Mosby Lifeline. 1994. 237]**PEER REVIEWED**

For basic treatment: Establish a patent airway. Suction if necessary. Watch for signs of respiratory insufficiency and assist ventilations if necessary. Administer oxygen by nonrebreather mask at 10 to 15 L/min. Monitor for pulmonary edema and treat if necessary. ... For contamination, flush eyes immediately with water. Irrigate each eye continuously with normal saline during transport. ... Do not use emetics. For ingestion, rinse mouth and administer 5 mL/kg up to 200 mL of water for dilution if the patient can swallow, has a strong gag reflex, and does not drool. Administer activated charcoal ... . /Ketones and related compounds/
[Bronstein, A.C., P.L. Currance; Emergency Care for Hazardous Materials Exposure. 2nd ed. St. Louis, MO. Mosby Lifeline. 1994. 237]**PEER REVIEWED**

Animal Toxicity Studies:

Evidence for Carcinogenicity:

CLASSIFICATION: D; not classifiable as to human carcinogenicity. BASIS FOR CLASSIFICATION: Based on no human carcinogenicity data and inadequate animal data. HUMAN CARCINOGENICITY DATA: None. ANIMAL CARCINOGENICITY DATA: Inadequate.
[U.S. Environmental Protection Agency's Integrated Risk Information System (IRIS) on methyl ethyl ketone (78-93-3) Available from: http://www.epa.gov/ngispgm3/iris on the Substance File List as of March 15, 2000]**PEER REVIEWED**

Non-Human Toxicity Excerpts:

THE SINGLE DOSE ORAL TOXICITY ... HAS BEEN DETERMINED TO BE 3.3 G/KG ... FOR RATS. MASSIVE DOSES MAY BE EXPECTED TO RESULT IN IRRITATION OF THE LUNG & ... /CNS DEPRESSION/.
[Patty, F. (ed.). Industrial Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New York: Interscience Publishers, 1963.

1732]**PEER REVIEWED**

Guinea pigs exposed to 3300 ppm for 13.5 hr showed no signs of intoxication. Exposure to 10,000 ppm for a similar period produced irritation of the eyes and nose within 4 min and /CNS depression/ between 4-5 hr. Exposure to 33,000 ppm for 200 min produced /CNS depression/ and death. Exposure to 100,000 ppm for 45-55 min produced /CNS depression/ after 10 min.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1753]**PEER REVIEWED**

Exposure /of rats/ to 2000 ppm /for 2 hr/ showed no apparent toxicity. Exposure to 8000 ppm killed 3 of 6 rats in 8 hr, while 16,000 ppm for 1 hr caused death of all the animals.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1753]**PEER REVIEWED**

EXPOSURE TO 1500 PPM OF **METHYL ETHYL KETONE (**MEK) ALONE FOR 7-9 WK DID NOT CAUSE PARALYSIS BUT DID ELEVATE PLASMA CHOLINESTERASE LEVELS IN MICE, RATS, & CHICKENS.
[COURI D ET AL; PROC ANNU CONF ENVIRON TOXICOL, 5TH, AMRL-TR-74-125: 109 (1974)]**PEER REVIEWED**

ANALYSIS OF PORPHYRIN CONTENT OF MURINE ERYTHROLEUKEMIA (MEL) CELLS INCUBATED WITH 2-**BUTANONE** SHOWED THAT INCR HEMOGLOBIN SYNTH WAS ACCOMPANIED BY ACCUM OF PORPHYRINS.
[EBERT PS ET AL; CHEM BIOL INTERACT 36 (1): 61 (1981)]**PEER REVIEWED**

The effects of the solvents n-hexane, **butanone** (**methyl ethyl ketone,** MEK) and a mixture of both in the intrapulmonary nerve system of rats were studied by light and electron microscopy. The alteration in the fine structures of the tissues consisted in a disseminated swelling of axons due to a striking multiplication of neurofilaments. Nonspecific axonal alterations could be demonstrated as well. The latter consisted in clusters of phospholipid material within the axoplasm of nerve fibers and the cytoplasm of Schwann cells plus an accumulation of glycogen granules in the axoplasm. Additionally, single degenerative changes of Schwann cells were observed.
[Schmidt R; Respiration 46 (4): 62-9 (1984)]**PEER REVIEWED**

METHYL ETHYL KETONE DELAYED MATCH-TO-SAMPLE DISCRIMINATION TASK IN THE JUVENILE BABOON & ALSO SLOWED RESPONSE TIMES & INCR EXTRA RESPONSES.
[GELLER I; NEUROBEHAV TOXICOL 1 (SUPPL 1): 9 (1979)]**PEER REVIEWED**

METHYL ETHYL KETONE WAS EVALUATED FOR EFFECTS ON A DELAYED MATCH TO SAMPLE DISCRIMINATION TASK IN THE JUVENILE BABOONS. THE ANIMALS WERE EXPOSED TO HALF THE THRESHOLD LIMIT VALUE (245 MG/CU M) FOR 24 HR PER DAY DURING A 7 DAY PERIOD. EACH EXPOSURE CONDITION AFFECTED ACCURACY OF PERFORMANCE MINIMALLY BUT RESULTED IN INCREASED AND DECREASED EXTRA RESPONSES DURING THE DELAY INTERVALS.
[GELLER I; PHARMACOL BIOCHEM BEHAV 11 (4): 401-6 (1979)]**PEER

REVIEWED**

Intraperitoneal injection of 750, 1500 or 2000 mg/kg **methyl ethyl ketone** to guinea pigs resulted in elevated serum ornithine carbamyl transferase (OCT) activity at the highest dose, where one of four animals died, and deposition of lipids in the liver with either 1500 or 2000 mg/kg was found.
[DiVincenzo GD et al; Am Ind Hyg Assoc J 34: 329 (1974)]**PEER REVIEWED**

Incubation of Ehrlich-Landschutz diploid ascites tumor cells in media containing 50 and 100 ppm **methyl ethyl ketone** resulted in the destruction of 10.5 and 14.0% of the cells. Control incubations lost only 4.2% of cells in the 5 hr period.
[Holmberg; Environ Res 7: 183 (1974)]**PEER REVIEWED**

Mutagenicity screening in Escherichia coli WP2, and Salmonella typhimurium strains TA1535, TA1537, TA1536 and TA1538 was negative.
[Smirasu Y; J Environ Poll Control 12: 407 (1976)]**PEER REVIEWED**

Pregnant rats inhaled 0, 400, 1000, or 3000 ppm of **methyl ethyl ketone** for 7 hr/day on days 6-15 of gestation. Maternal toxicity evidenced by decreased weight gain and increased water consumption was seen among rats exposed to 3000 ppm. Fetotoxicity (increased incidence of 2 minor skeletal variants) was observed among litters of rats exposed to 3000 ppm.
[Deacon MM et al; Toxicol Appl Pharmacol 59 (3): 620-2 (1981)]**PEER REVIEWED**

Groups of rats were exposed to 100 ppm hexane, 200 ppm **methyl ethyl ketone (**MEK), or fresh air in an exposure chamber 12 hr daily for 24 weeks. Body weight, motor nerve conduction velocity, distal motor latency, and mixed conduction velocities were measured before exposure and after 4, 8, 12, 16, 20, and 24 wk exposure. ... Exposure to 200 ppm MEK significantly increased motor nerve conduction velocity, and mixed conduction velocities and decreased distal motor latency after 4 week exposure; but at a later stage no significant changes were found. Mixed exposure to 100 ppm hexane and 200 ppm MEK significantly decreased distal motor latency after 4 week exposure and decreased motor nerve conduction velocity and mixed conduction velocities after 20 and 24 week exposure.
[Takeuchi Y et al; Br J Ind Med 40 (2): 199-203 (1983)]**PEER REVIEWED**

Groups of Sprague-Dawley rats were exposed, by inhalation to ... **methyl ethyl ketone (**800 ppm, 2345 mg/cu m) ... for 4 weeks. Increased liver weights and liver-to-body weight ratios were observed. **Methyl ethyl ketone** depressed the formation of 2 metabolites of androstenedione but did not alter the concentration of cytochrome p450 in companion in vitro microsomal metabolism studies.
[Toftgard R et al; Scand J Work Environ Health 7 (1): 31-7 (1981)]**PEER REVIEWED**

Vapors in concn of 1000 ppm or 3000 ppm were embryotoxic and fetotoxic in rats causing acaudia, imperforate anus, and brachygnathia, as well as retardation of fetal development.
[Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984.,p. II-185]**PEER REVIEWED**

Testing of a drop on rabbit eyes indicates moderate reversible injury, graded 5 on a scale of 1-10. The

compound was tested externally on the eyes of rabbits, and, according to the degree of injury observed after 24 hours, rated on a scale of 1 to 10. The most severely injurious substances have been rated 10.
[Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986. 617]**PEER REVIEWED**

Male and female Fischer 344 rats were exposed to 0, 1250, 2500, or 5000 ppm **methyl ethyl ketone (**MEK) vapors 6 hr/day, 5 day/wk for 90 days. The 90 day exposures had no adverse effect on the clinical health or growth of male or female rats except for a depression of mean body wt in the 5000 ppm exposure group. The 5000 ppm animals had a slight but significant increase in liver weight, liver weight/body weight ratio, and liver weight/brain weight ratio at necropsy. Serum glutamic-pyruvic transaminase (SGPT) activity in the 2500 ppm female rats was elevated while the 5000 ppm female rats exhibited significantly decreased serum glutamic-pyruvic transaminase SGPT activity. In addition, alkaline phosphatase, potassium, and blood glucose values for the 5000 ppm female rats were increased. ...
[Cavender FL et al; Fundam Appl Toxicol 3: 264-70 (1983)]**PEER REVIEWED**

Chinese hamsters were exposed to ... **methyl ethyl ketone ...** known to be a strong inducer of aneuploidy in the yeast Saccharomyces cerevisiae. ... Solvent yielded negative results in the micro-nucleus test.
[Basler A; Mutat Res 174 (1): 11-13 (1986)]**PEER REVIEWED**

... Cultures of mature organotypic cord ganglia were extracted from fetal mouse spinal cord with the attached dorsal root. MEK at 300 ug/ml nutrient fluid was added to cultures for periods of up to 7 weeks. Cultures were examined under microscope twice weekly for morphological changes and were sampled at 3, 5, and 7 weeks for electron microscopy. Treated cultures remained viable for the 7 week exposure period. After 6 to 7 weeks of exposure, distinct intraaxonal inclusion occurred along proximal and distal internodes of occasional sensory peripheral nerves (PNS). The structures lengthened and darkened throughout the exposure period and were often associated with axoplasmic granularity. The earliest change in cytoplasm was dispersion of Nissl bodies, which resulted in excessive numbers of free ribosomes or polyribosomal changes. There was a distension of neuronal cisternal systems. By week 5 there were abnormal amounts of smooth or agranular endoplasmic reticulum which appeared swollen with a translucent material. A swollen agranular recticulum was often associated with foci of axoplasmic debris. By week 7, intra-axonal cores of debris and myelin whorls were documented in 25% of the central nervous system and sensory perpipheral nerves axons examined ultrastucturally. ...
[Veronesi B; Neurotoxicology 5 (4): 31-43 (1984)]**PEER REVIEWED**

Chemical test results for cytogenetic effects in Chinese hamster ovary cells ... were negative for both chromosome aberrations and sister chromatid exchanges.
[NTP; Fiscal Year 1987 Annual Plan p.87 (1987) NTP-87-001]**PEER REVIEWED**

An oral dose of 1.5 g/kg to rats resulted in a 63% incr in liver triglycerides after 16 to 23 hr, but did not alter liver histology or incr either of two enzymes, serum glutamic-pyruvic transaminase (alanine transferase (ALT)) and hepatic glucose-6-phosphatase ... Much smaller acute ip doses (0.049 to 0.194 g/kg) to rats appeared not to damage the liver. A single oral dose (15 mmol/kg) of MEK did not affect the hepatobiliary function of rats over an observation period of 10 to 96 hr. ... A graded series of single doses of MEK to guinea-pigs revealed high sensitivity to small changes in dosage. The low dose (0.75

g/kg) appeared to produce no liver damage, whereas 1.5 g/kg produced slight liver damage and 2.0 g/kg produced major liver damage. These results also suggest that guinea-pigs and rats may be equally sensitive to MEK in terms of liver damage even though guinea-pigs survive acute exposure to higher concn of MEK vapor than do rats ... .
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.58 (1993)]**PEER REVIEWED**

Consistent incr in the frequency of food-reinforced lever pressing by rats were detected at MEK exposures as low as 74 mg/cu m (25 ppm) for 2 hr. ... Vestibulo-ocular effects were detected during continuous iv admin of MEK for 1 hr via the caudal vein at a dosage as low as 0.005 g/kg/min ... this dosage is roughly equivalent to inhalation of 2,700 mg/cu m (900 ppm). ... Exposure of mice to 885 mg/cu m (300 ppm) for 30 min did not significantly alter schedule-controlled responses, whereas concn-related suppression of response occurred at consecutive incr concn (for 30 min) ranging from 2,950 to 29,500 mg/cu m (1,000 to 10,000 ppm) ... .
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.67 (1993)]**PEER REVIEWED**

In skin irritation studies, a small dose (8 mg) applied to clipped skin and covered by an impervious plastic film for 24 hr ... produced only minor irritation in male New Zealand albino rabbits. ... A dose of 400 mg applied to the clipped dorsal skin of restrained albino rabbits in a gauze patch produced mild to moderate irritation in some cases. ... Neat MEK (0.1 mL) applied to the clipped skin of the flanks of guinea pigs and rabbits daily for 10 days and left uncovered caused erythema and edema after 24-72 hr. These effects were more marked in rabbits ... .
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.67 (1993)]**PEER REVIEWED**

The results of studies on eye irritation in rabbits are inconsistent. ... 0.005 mL (4 mg) created a severe chemical burn in the rabbit eye, whereas /another/ ... study ... reported less severe irritant effects from the larger dose of 0.1 mL (80 mg). Data from ... /another/ study ... were also inconsistent but indicated that a dose of 0.1 mL (80 mg) produced minimal to moderate eye irritation. Undiluted MEK was used in all three studies ... /however different ocular grading scales were employed/. In all studies irritation disappeared or was markedly reduced by 7 days after treatment. Opaque corneas were apparent following exposure of guinea-pigs to 295,000 mg MEK/cu m (100,000 ppm) for 30 min; recovery from this effect was complete in 4-8 days ... .
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.68 (1993)]**PEER REVIEWED**

Female rats exposed to 14,750 mg/cu m (5,000 ppm) 6 hr/day, 5 days/wk for 90 days showed only slightly incr liver weight, slightly decr brain and spleen weights, and slightly altered blood chemistry in comparison with controls. Male rats receiving this exposure showed only a slightly incr liver weight. At lower concn of MEK (3,688 and 7,375 mg/cu m (1,250 and 2,500 ppm)) there was only slightly incr liver weight for female rats and no significant differences for males in comparison with controls ... . In another subchronic inhalation study ... male and female rats were exposed to MEK concn of 3,700, 7,430 and 14,870 mg/cu m (1,254, 2,518, and 5,041 ppm) 6 hr/day, 5 days/wk for 90 days. No significant effects on food consumption, eyes or nervous system were observed. In addition, MEK-induced morphological changes in the central or peripheral nervous system were detected.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.68

(1993)]**PEER REVIEWED**

In the cat, injection of 150 mg MEK (99.98% pure) per kg, twice a day, 5 days/wk, for up to 8.5 months, into subcutaneous tissue produced abscesses, skin ulceration and generalized weakness but no evidence of damage to the nervous system ... .
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.73 (1993)]**PEER REVIEWED**

... examined the vestibulo-oculomotor reflex (VOR) during iv infusion of MEK into the caudal veins of 18 female Sprague-Dawley rats. The threshold for depression of the VOR was an infusion rate of 70 umol/kg (0.005 g/kg per min) for 1 hr (total dose 30 mg) and the assoc arterial blood level was 1.4 mmol/L. General depression of the central nervous system followed depression of the VOR.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.74 (1993)]**PEER REVIEWED**

... groups of 10 virgin female Swiss CD1 mice and 33 plug-positive (day 0) females were exposed by inhalation on gestation days 6-15 to mean concn of 1174 ... 2980 ... and 8909 ... mg/cu m. ... There was no evidence of maternal toxicity, although there was a slight, treatment-related incr in liver/body weight ratios that was significant at the highest dose level. Mild fetal toxicity was evident at this maternal dose level as a reduction in mean fetal body weight, statistically significant for males. There was no incr in the incidence of intrauterine death, but there was an incr dose-related incidence of misaligned sternebrae, statistically significant at the highest dose level. There were no significant incr in the incidence of malformations, although there were several malformation in one litter (cleft palate, fused ribs, missing vertebrae, syndactyly) in treated groups but not in the control group nor in contemporary control data.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.77 (1993)]**PEER REVIEWED**

... conducted mutagenicity studies on MEK. The test systems comprised the Salmonella/microsome (Ames) assay, the L5178/TK+/- mouse lymphoma (M/L) assay, the BALB/3T3 cell transformation (CT) assay, unscheduled DNA synthesis (UDS) and the micronucleus test. MEK was not found to be genotoxic in these assays.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.80 (1993)]**PEER REVIEWED**

The effect of MEK on the alarm behavior of social insects has been studied. It was considered inactive in producing alarm behavior in the ant Iridomyrmex preinosus ... the harvester ant Pogonomyrmex badius ... and the honeybee Apis Mellifera ... .
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.96 (1993)]**PEER REVIEWED**

The developmental effects observed at an MEK vapor concentration of 3000 ppm were reexamined. Pregnant Sprague-Dawley rats were exposed to 400, 1000, or 3000 ppm of MEK for 7 hr/day on days 6 to 15 of gestation. There were no effects on maternal liver weight; however, a significant decrease in maternal body weight gain was observed in the animals exposed to 3000 ppm of MEK. In addition, none of the exposures affected the pregnancy rate, the number of implantations or fetal resorptions, the litter size, or the fetal body weight. Unlike the initial study, there were no gross or soft-tissue malformations at any exposure level; however, the 3000-ppm exposure caused a significant increase in the incidence of delayed skeletal ossifications (skull and neck) and an increase in the incidence of extra lumbar ribs. /It

was/ concluded that MEK was not embryotoxic or teratogenic and only slightly fetotoxic in the rat at exposure concentrations of 3000 ppm.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1759]**PEER REVIEWED**

Groups of pregnant and nonpregnant mice were exposed to MEK vapor concentrations of 400, 1000, or 3000 ppm for 7 hr/day for 10 consecutive days (for pregnant mice, days 6 to 15 of gestation). The nonpregnant and pregnant mice showed no differences in sensitivity to the MEK exposures. The maternal body weight gain, extragestational weight gain, uterine weight, pregnancy rate, and implantation ratio were not affected by exposure to MEK vapors relative to control. The 3000-ppm exposure did, however, result in a relative increase in maternal liver and kidney weight. The percentage of live fetuses, resorptions, and dead fetuses per litter was also unaffected by the treatment. A concentration-related decrease in fetal weight was observed for both the male and females. Although there were no statistically significant increases in the number of malformed fetuses per litter, there were several atypical malformations (cleft palate, fused ribs, missing vertebrae, and syndactyly) not often found in control litters. A statistically significant increase in the incidence of misaligned sternebrae was observed in the fetuses exposed to 3000 ppm of MEK. No developmental or maternal effects were observed at vapor concentrations of 1000 ppm or less. After considering the results from the present study together with results obtained in rats, the authors concluded that MEK vapors caused mild developmental toxicity at concentrations that caused maternal toxicity.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1758]**PEER REVIEWED**

Non-Human Toxicity Values:

LD50 Rat oral 2.9 (95% C.I. 2.3-3.5) g/kg /From table/
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.59 (1993)]**PEER REVIEWED**

LD50 Rat (female) oral 5.52 (95% C.I. 4.50-6.80) g/kg /From table/
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.59 (1993)]**PEER REVIEWED**

LD50 Mouse (male) oral 3.14 + or - 0.67 g/kg /From table/
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.60 (1993)]**PEER REVIEWED**

LC50 (45 min) Mouse (male) inhalation 205,000 + or - 32,500 mg/cu m (69,500 + or - 11,000 ppm) /From table/
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.60 (1993)]**PEER REVIEWED**

LC50 (4 hr) Rat (male) inhalation 34,500 mg/cu m (11,700 ppm) /From table/
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.61 (1993)]**PEER REVIEWED**

LD50 (24 hr) Mouse (male) ip 1.66 + or - 0.74 g/kg /From table/

[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.63 (1993)]**PEER REVIEWED**

LD50 (24 hr) Rat (female) ip 1.554 (95% CI 1.229-1.966) g/kg /From table/
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.63 (1993)]**PEER REVIEWED**

LD50 (14 day) Rat (female) ip 0.607 (95% C.I. 0.486-0.748 g/kg /From table/
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.63 (1993)]**PEER REVIEWED**

LD50 (14 days) Rabbit (male) dermal >8 g/kg /From table; 24-hr occluded exposure duration/
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.64 (1993)]**PEER REVIEWED**

Ecotoxicity Values:

LC50 Lepomis macrochirus (bluegill) 5,640-1,690 mg/l 24 to 96-hr /Conditions of bioassay not specified/
[Verschueren, K. Handbook of Environmental Data on Organic Chemicals. 3rd ed. New York, NY: Van Nostrand Reinhold Co., 1996. 1283]**PEER REVIEWED**

LC50 Artemia salina (brine shrimp) 1,950 mg/L 24-hr /From table; bottles not sealed and may have lost MEK during experiment; water pH, temp, and hardness not specified/
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.97 (1993)]**PEER REVIEWED**

LC50 Daphnia magna (water flea) <520 mg/L 48-hr /From table; pH 8 and hardness 173; temp not specified/
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.97 (1993)]**PEER REVIEWED**

LC50 Daphnia magna (water flea) 1382 (95% C.I. 918-3349) mg/l 48-hr /From table; pH 7.21, temp 21.0-23.0 deg C, hardness 38 mg/L calcium carbonate /
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.97 (1993)]**PEER REVIEWED**

LC50 Daphnia magna (water flea) 8890 mg/l 24-hr /From table; pH 7.6-7.7, temp 20-22 deg C, hardness 16 deg (German)/
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.97 (1993)]**PEER REVIEWED**

LC50 Lebistes reticulatus (guppy) 5700 mg/l 24-hr /From table; pH not given, temp 20 deg C, hardness 27.5 mg/L CaCl2/
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.98 (1993)]**PEER REVIEWED**

LC50 Pimephales promelas (fathead minnow) 3200 mg/L 96 hr /From table; pH 7.5, temp 25 deg C, hardness 42.2 mg/L calcium carbonate /

[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.99 (1993)]**PEER REVIEWED**

LC50 Lepomis macrochirus (bluegill sunfish) 4467 mg/l 96-hr /From table; pH 7.93, temp 21 deg C, hardness 240 mg/l calcium carbonate /
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.99 (1993)]**PEER REVIEWED**

LC50 Gambusia affinis (mosquito fish) 5600 mg/l 96-hr /From table; pH 7.8-8.3, room temp, hardness not specified/
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.99 (1993)]**PEER REVIEWED**

LC50 Carassius auratus (goldfish) >5000 mg/l 24-hr /From table; pH 7.0, temp 20 deg C, hardness 100 mg/l/
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.99 (1993)]**PEER REVIEWED**

TSCA Test Submissions:

The ability of **methyl ethyl ketone** to induce morphological transformation in the BALB/3T3 mouse cell line (Cell Transformation Assay) was evaluated both in the presence and absence of added metabolic activation by Aroclor-induced rat liver S9 fraction. Based on preliminary clonal toxicity determinations (exposure time=2 hrs), **methyl ethyl ketone,** diluted with phosphate buffered saline, was tested at 18, 13 and 9ul/ml in the absence of metabolic activation, with cell survival ranging from 93.3% to 51.1% relative to the solvent control. Assays with metabolic activation were tested at 10, 8 and 6ul/ml (exposure time=2 hrs), with cell survival ranging from 85.7% to 67.3%. None of the tested concentrations produced significantly greater transformation frequencies ($p > 0.05$, Modified Poisson Distribution) relative to the solvent control.
[Microbiological Associates Inc.; Activity of Methyl Ethyl Ketone in the Morphological Transformation Assay using BALB/3T3 Mouse Embryo Cells, Final Report, (1984), EPA Document No. 40-8444072, EPA Fiche No. OTS0507470] **UNREVIEWED**

An inhalation teratology study was conducted with pregnant Sprague-Dawley rats (25/group) receiving whole body exposure to **methyl ethyl ketone** in a dynamic air flow chamber, 7 hours/day on days 6 through 15 of gestation. There was no effect of treatment for all animals as indicated by clinical observations, absolute or relative liver weights, food consumption, number of pregnancies, and mortality. Maternal toxicity was evident by statistical differences between high dose groups and controls for: maternal body weights, maternal body weight gain and water consumption. The average number of live fetuses per litter, incidence of resorption rates, fetal body weight or crown-rump length were not significantly affected by treatment. Significant differences were observed between the fetuses of the control and high dose group for skeletal variations, but no significant external or soft-tissue alterations were observed in any of the fetuses of treated females.
[Dow Toxicology Research Laboratory; Teratologic Evaluation of Inhaled Methyl Ethyl Ketone in Rats, (1979), EPA Document No. 878210652, Fiche No. OTS0206178] **UNREVIEWED**

The ability of **methyl ethyl ketone** to induce specific locus mutations at the TK locus in cultured L5178Y mouse lymphoma cells (Mouse Lymphoma Mutagenicity Assay) was evaluated in the presence and absence of Aroclor-induced rat liver S9 metabolic activation. Based on preliminary toxicity tests, 10 nonactivated cultures treated with 12, 8.9, 6.7, 5.0, 3.8, 2.8, 2.1, 1.6, 1.2 and 0.89ul/ml were cloned, producing a range of 46 - 122% total growth. Ten S9-activated cultures treated with 8.9, 6.7, 5.0, 3.8, 2.8, 2.1, 1.6, 1.2, 0.89 and 0.67ul/ml were cloned, producing a range of 30 - 116% total growth. None of the cultures that were cloned produced mutant frequencies which were significantly greater than the mean mutant frequency of the solvent controls (DMSO, acetone).
[Microbiological Associates Inc.; L5178Y TK +/- Mouse Lymphoma Mutagenicity Assay, Final Report, (1984), EPA Document No. 40-8444072, Fiche No. OTS0507470] **UNREVIEWED**

The mutagenicity of **methyl ethyl ketone** was evaluated in Salmonella tester strains TA98, TA100, TA1535, TA1537 and TA1538 (Ames Test), both in the presence and absence of added metabolic activation by Aroclor-induced rat liver S9 fraction. Based on the results of the preliminary bacterial toxicity determinations, **methyl ethyl ketone,** diluted with DMSO, was tested for mutagenicity at concentrations up to 32 ul/plate (presence metabolic activation) and 16 ul/plate (absence metabolic activation) using the preincubation technique. **Methyl ethyl ketone** did not cause a reproducible positive response in any of the bacterial tester strains, either with or without metabolic activation.
[Microbiological Associates, Inc.; Salmonella/Mammalian-Microsome Preincubation Mutagenicity Assay (Ames Test), (1984), EPA Document No. 40-8444072, Fiche No. OTS0507470] **UNREVIEWED**

The mutagenicity of **methyl ethyl ketone (**MEK) was evaluated in bacterial tester strains E. coli WP2 and WP2uvrA and Salmonella TA98, TA100, TA1535, TA1537 and TA1538, and the yeast Saccharomyces cerevisiae tester strain JD1, both in the presence and absence of added metabolic activation by Aroclor-induced rat liver S9 fraction. Based on preliminary bacterial toxicity determinations, MEK, diluted with DMSO, was tested for mutagenicity at concentrations up to 4000 ug/plate in the bacterial tests and 5000 ug/plate in the yeast tests using the agar overlay method. MEK did not cause a positive response in any of the bacterial tester strains, either with or without metabolic activation.
[Shell Sittingbourne Research Centre; Toxicity Studies with Chemical Solvents: Short-Term in Vitro Tests for Genotoxic Activity with Methyl Ethyl Ketone. (1982), EPA Document No. 878210125, Fiche No. OTS0206206] **UNREVIEWED**

Methyl ethyl ketone was evaluated for the ability to increase the incidence of micronucleated polychromatic erythrocytes in bone marrow of male and female CD-1 mice treated by single i.p. injection (Micronucleus Test). Groups of 10 mice (5 male, 5 female) were sacrificed 12, 24 and 48 hours following injection of **methyl ethyl ketone** in corn oil at a dose of 1.96 ml/kg body weight (calculated LD20 dose). The ratio of normochromatic to polychromatic erythrocytes were not significantly different ($p > 0.05$, ANOVA) in the treated groups compared with vehicle controls, regardless of sacrifice time. The incidence of micronucleated polychromatic erythrocytes was increased above the vehicle control 24 hours after administration, but was not considered statistically significant when compared to all treatment and vehicle control groups regardless of sacrifice time ($p > 0.05$, ANOVA).
[Microbiological Associates Inc.; Activity of Methyl Ethyl Ketone in the Micronucleus Cytogenetic Assay in Mice, Final Report, (1984), EPA

Document No. 40-8444072, Fiche No. OTS0507470] **UNREVIEWED**

The effects of **methyl ethyl ketone** were examined in the rat hepatocyte primary culture/DNA repair assay. Based on preliminary toxicity tests, **methyl ethyl ketone** was tested at concentrations of 5.0 (relative toxicity 74.67%), 2.5, 1.0, 0.5, 0.1 or 0.01 ul/ml (relative toxicity 6.67%). None of the tested concentrations caused a significant increase in unscheduled DNA synthesis over the solvent control (DMSO).
[Microbiological Associates Inc.; Unscheduled DNA Synthesis in Rat Primary Hepatocytes, Final Report, (1984), EPA Document No. 40-8444072, Fiche No. OTS0507470] **UNREVIEWED**

The ability of **methyl ethyl ketone** to cause chromosome aberrations was evaluated in cultured rat (strain not reported) liver cell line. Based on preliminary toxicity determinations, rat liver cultures were exposed to 250, 500 or 1000 ug/ml and incubated for 24 hours. Two hours prior to the end of incubation, colcemid was added and at the end of incubation period 100 cells from each culture were analyzed. No increase (statistical analysis not reported) in the frequency of chromatid gaps, chromatid breaks or total chromatid aberrations were observed in any of the cultures.
[Sittingbourn Research Center; Toxicity Studies with Chemical Solvents: Short Term In Vitro Tests for Genotoxic Activity with Methyl Ethyl Ketone, (1982), EPA Document No. 878210125, Fiche No. OTS0206206] **UNREVIEWED**

Metabolism/Pharmacokinetics:

Metabolism/Metabolites:

METHYL ETHYL KETONE (MEK) OCCURS ... IN NORMAL HUMAN URINE & ... HAS POSSIBLE DIETARY ORIGIN; ITS MORE PROBABLE PRECURSOR IS ALPHA-METHYLACETOACETIC ACID. LIKE OTHER KETONES ... MEK IS REDUCED ... IN THE BODY. ONLY 30-40% ... IS ELIMINATED IN EXPIRED AIR ... .
[Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965. 422]**PEER REVIEWED**

IT HAS BEEN SHOWN TO INCREASE THE GLUCURONIC ACID OUTPUT ... & URINE OF RABBITS RECEIVING IT HAS BEEN STATED ... TO CONTAIN THE GLUCURONIDE OF 2-BUTANOL.
[Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965. 422]**PEER REVIEWED**

GUINEA PIGS WERE GIVEN SINGLE 450 MG/KG IP DOSES OF **METHYL ETHYL KETONE (**MEK). MEK PRODUCED 2-BUTANOL, 3-HYDROXY-2-**BUTANONE**, & 2,3-BUTANEDIOL.
[DIVINCENZO GD ET AL; TOXICOL APPL PHARMACOL 36 (3): 511 (1976)]**PEER REVIEWED**

Uptake of oxygen by Mycobacterium smegmatis 442, and Corynebacterium sp during metabolism of 1 ul of **methyl ethyl ketone (**MEK) in Warburg respirometers, was 196 and 266 ul of oxygen respectively.
[Lukins HB, Foster JW; J Bacteriol 85: 1076-87 (1963)]**PEER REVIEWED**

Milk cultures of five Leuconostoc dextranicum strains were capable of reducing **methyl ethyl ketone (**MEK) to 2-butyl alcohol.
[Keenan TW; Appl Microbiol 16: 1881-5 (1968)]**PEER REVIEWED**

Resting cells of Lactobacillus brevis 24 reduced **methyl ethyl ketone (**MEK) quantitatively to 2-butyl alcohol when incubated in phosphate buffer for 24 hr at 30 deg C.
[Keen AR et al; J Dairy Res 41: 249-57 (1974)]**PEER REVIEWED**

Rats were given a single oral dose of **methyl ethyl ketone (**MEK). The blood concn of MEK and metabolites 4 hr after dosing were: MEK (94.1 mg/100 ml); 2-butanol (3.2 mg/100 ml); 3-hydroxy-2-butanol (2.4 mg/100 ml) and 2,3-butanediol (8.6 mg/100 ml). Blood concn of the parent compound and metabolites 18 hr after dosing with MEK were: MEK (6.2 mg/100 ml); 2-butanol (0.6 mg/100 ml); 3-hydroxy-2-**butanone** (1.4 mg/100 ml); and 2,3-butanediol (25.6 mg/100 ml).
[Dietz FKJ, Traiger GJ; Toxicology 14: 209-14 (1979)]**PEER REVIEWED**

MEK has been reported to be a metabolic end product of natural gas (methane 88%, ethane 5%, propane 5%, iso-butane 2%, with traces of t-butyl mercaptan and methyl acrylate) inhaled for 2 hr by ICR mice ... In an in vivo study of the metabolism of propane, n-butane and iso-butane inhaled for 1 hr by ICR mice, it was found that n-butane gave rise to sec-butanol and MEK ... In vitro studies showed that mouse liver microsomal preparations metabolized n-butane to sec-butanol, the precursor of MEK ... Inhalation by male Sprague-Dawley rats of sec-butanol at concn of 5900 mg/cu m (2000 ppm) for 3 days or 1475 mg/cu m (500 ppm) for 5 days caused marked enzyme induction of cytochrome P-450 in liver and kidney but other butanol isomers did not have this effect ... The authors concluded that the mechanism of induction was via the sec-butanol metabolite MEK.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.51 (1993)]**PEER REVIEWED**

... the toxic effects of MEK and 2-butanol were essentially identical in rats, and that 2-butanol was rapidly oxidized to MEK. ... identified the metabolites of MEK in guinea pigs as 2-butanol, 3-hydroxy-2-**butanone** and 2,3-butanediol. They hypothesized that the metabolism followed both oxidative and reductive pathways, with the latter leading to the production of 2-butanol.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.52 (1993)]**PEER REVIEWED**

In rats exposed by inhalation to 1760 mg MEK/cu m (600 ppm), there were only marginal effects on microsomal cytochrome P-450 activities ... However, a daily dose of 1.4 mL MEK per kg for 3 days incr the amounts of ethanol- and phenobarbital-inducible cytochromes P-450 ...
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.53 (1993)]**PEER REVIEWED**

In a study on male Sprague-Dawley rats, pretreatment with MEK elevated total microsomal cytochrome P-450 and NADPH-dependent cytochrome-c-reductase, the rates of oxidation of N-nitrosodimethylamine, benzphetamine and pentoxyresorufin, and also the levels of immunoreactive protein for both P-450 isozymes ... In a study of hepatotoxicity in rats, ... found that MEK incr liver cytochrome P-450 content (33-86%) and glutathione-S-transferase (GST) activity (42-64%) but had no effect on serum glutamate dehydrogenase (GLDH) activity. ... studied the effects on hepatic cytochrome P-450 activities of repeated daily doses of 1.87 mL/kg given by gavage to male Fischer-344 rats. The activity of 7-ethoxy coumarin-O-deethylase was incr by up to 500% after 1 to 7 days of MEK treatment,

but there was practically no change in benzphetamine-N-demethylase activity. In another study in male Sprague-Dawley rats, admin of MEK by gavage cause an incr in hepatic acetanilide hydroxylase and a marginal incr in aminopyrine-N-demethylase activities ... .
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.53 (1993)]**PEER REVIEWED**

MEK has been identified as a minor but normal constituent of urine ... serum and urine of diabetics ... and expired air ... . Its production in the body has been attributed to isoleucine catabolism ... studies ... indicate that the same metabolites are produced and excreted in humans as in experimental animals. ... further indicated that in an inhalation exposure to 590 mg MEK/cu m (200 ppm) the calculated areas under the curves of blood solvent concn versus time (AUC) for MEK and 2,3-butanediol were equal, which suggests that MEK is almost completely transformed to 2,3-butanediol. The bulk of MEK absorbed thus enters the general metabolism and is transformed to simple compounds like carbon dioxide and water.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.55 (1993)]**PEER REVIEWED**

Absorption, Distribution & Excretion:

Measurable (2.54 to 13 ug/l) quantities of **methyl ethyl ketone** appeared in expired air of adult humans 3 min following dermal exposure to 100 ml **methyl ethyl ketone** applied to 91.5 sq cm of skin.
[Wurster; J Pharm Sci 54: 554 (1965)]**PEER REVIEWED**

Ketones are readily absorbed through the intact skin. Usually they are rapidly excreted ... in the expired air. /Ketones/
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 1170]**PEER REVIEWED**

Workers occupationally exposed to **methyl ethyl ketone (**MEK) were examined. ... Workers exposed to 300 micrograms per liter MEK, the aveolar concn was 30% of the environmental concn. Lung uptake averaged 1.05 mg/min. The blood concn of MEK ranged from 842 to 9573 ug/l, with a mean of 2630 ug/l. Blood concn of MEK were strongly correlated with alveolar concn. MEK was more soluble in heart and muscle tissue than in lung tissue or fat. Urinary MEK excretion ranged from 120 to 1120 mg/l, with a mean of 487 mg/l. ... MEK was not persistent in the tissues. ... Urinary excretion of MEK and acetylmethylcarbinol are only around 0.1% of MEK lung absorption, the main pathway through which MEK is eliminated is unknown.
[Perbellini L et al; Intern Arch Occup Environ Health 54 (1): 73-81 (1984)]**PEER REVIEWED**

ALTHOUGH ABSORPTION ... THROUGH THE SKIN MAY OCCUR, IT HAS BEEN SHOWN THAT IT IS LOW IN TOXICITY BY THIS ROUTE.
[Patty, F. (ed.). Industrial Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New York: Interscience Publishers, 1963. 1732]**PEER REVIEWED**

Percutaneous absorption of MEK appears to be rapid ... MEK was present in the exhaled air of human subjects within 2.5-3.0 min after it was applied to normal skin of the forearm, and the concn of MEK in

exhaled air reached a plateau in 2-3 hr. The rate of absorption was controlled mainly by the moisture content of the skin. With dry skin, absorption was slow, and it took 4-5 hr for the concn of MEK in expired air to attain a plateau. With moist skin, absorption was very rapid initially. MEK was detected in expired air in measurable concn within 30 sec after an application of MEK to the forearm, and a max concn in expired air, averaging 4X the plateau level for normal and dry skin, was achieved in 10-15 min.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.49 (1993)]**PEER REVIEWED**

The absorption of MEK via the lungs was examined ... in a study of workers exposed in industrial workplace. The MEK concn in alveolar and expired air correlated significantly with the environmental concn, and averaged 30% of the latter. In more recent studies ... values for pulmonary absorption ranging from 41.1% to 55.8% were obtained. ... Deeper inhalation incr the alveolar volume relative to the dead space (the non-alveolar volume of the respiratory system), and thus incr the apparent absorption ... .
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.49 (1993)]**PEER REVIEWED**

Results of studies ... indicated a rapid transfer of MEK vapor into the blood stream. ... the concn of MEK in the blood and urine were significantly correlated with the environmental concn, indicating rapid transfer to the blood and thence to other tissues. In human volunteer subjects, exercise during exposure markedly incr the MEK level in blood in comparison with sedentary behavior ... indicating that the blood MEK level also depended on the rate of uptake. ... also found significant correlations between environmental levels of MEK and amounts excreted in the urine of exposed workers. The concn of MEK in urine rose from essentially 0 to 70% of its max value during the first 2 hr of an 8-hr shift ... .
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.50 (1993)]**PEER REVIEWED**

... studied biological monitoring of occupational exposure to MEK in 67 healthy male workers employed in plastic bag or video-tape production. Their ages ranged between 18 and 52 yr with an average working experience of 8.6 yr. for the majority of the workers, atmospheric MEK concn were in the range of 30-885 mg/cu m (10-300 ppm). MEK concn in urine, blood and exhaled air were measured once/week at the end of a shift. About 10% of absorbed MEK was eliminated in the exhaled air. Following exposure to 590 mg/cu m (200 ppm), the urinary concn was 5.1 umol/L or 4.11 mg/g creatinine. The correlation coefficients between atmospheric MEK concn and end-of-shift urine, blood and exhaled air were 0.89, 0.85, and 0.79, respectively. The authors also reported good correlation between blood and urinary MEK ... and between blood and exhaled air concn ... but poor correlation between exhaled air and urinary MEK concn.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.50 (1993)]**PEER REVIEWED**

In male rats given a large MEK dose (1505 or 1690 mg/kg) in water, blood concn reached maxima of 0.95 and 0.94 mg/mL 4 hr after ingestion and subsequently declined sharply, indicating protracted absorption of this dose from the GI tract ... .
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.51 (1993)]**PEER REVIEWED**

... intraperitoneal injection of MEK in research on metabolism and toxicity, suggest that absorption from the peritoneal cavity is rapid.

[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.51 (1993)]**PEER REVIEWED**

The distribution of MEK in human tissues was examined ... in two solvent-exposed workers who died suddenly of heart attacks at the workplace. The results of this study ... indicate that the solubility of MEK is similar for all tissues. ... With a blood/air partition coefficient of 202, MEK can reach equilibrium concn in a compartment in about 3 min. Distribution volumes were 6.0 for vessel-rich tissues, 39.6 for muscle and 12.8 for fat. Biological half-lives for the same tissues were 0.8, 21.8 and 23.3 min, respectively.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.51 (1993)]**PEER REVIEWED**

The results of in vitro measurements at 37 deg C of human tissue-gas partition coefficients, obtained by exposing samples of blood and tissue to a known concn of MEK ... The partition coefficients ranged from 96 to 162, but did not exceed 111, with the exception of whole blood (125), blood plasma (133) and fat (162). Other blood-gas partition coefficients measurements for MEK are 202 ... and 215 ... .
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.51 (1993)]**PEER REVIEWED**

... provided evidence that MEK can enter the liver of rats and guinea-pigs, and ... reported that it can cross the placenta and enter the human fetus.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.51 (1993)]**PEER REVIEWED**

MEK and its metabolites are excreted by the lungs and kidneys. ... only 3% of the calculated absorbed dose during a 4-hr exposure to 590 mg MEK/cu m (200 ppm) was secreted unchanged in the exhaled air of volunteers after the exposure. The fractional elimination of unchanged substance however depends on the efficiency of metabolic clearance. Since metabolic saturation for MEK in humans begins at relatively low levels (about 100 ppm) of exposure ... proportionally greater amounts of MEK would be expected to be excreted via the lungs (and kidneys) at high exposure levels.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.55 (1993)]**PEER REVIEWED**

Relatively little of absorbed MEK is excreted unchanged via the kidneys; a study of occupationally exposed workers revealed that it is less than 0.1% of the alveolar uptake ... In a similar study of workers occupationally exposed to a mixture of solvents, the excretion of MEK and a major recognizable metabolite, 3-hydroxy-2-**butanone**, was 0.1% of alveolar uptake ... The concentrations of both MEK and 3-hydroxy-2-**butanone** in urine were significantly correlated with the environmental level of MEK. Other metabolites of MEK, 2-butanol or 2,3-butanediol ... identified in the serum of guinea pigs, were not detected in the urine of the exposed workers. ... however ... human excretion of 2,3-butanediol was individually variable but averaged 2% of the absorbed MEK. The urinary excretion of 2-butanol, a minor metabolite of MEK was examined ... clearance of 2-butanol admin by gavage in rabbits was about 14% of the admin dose and in the form of a glucuronide.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.55 (1993)]**PEER REVIEWED**

Absorption of methylethylketone is rapid via inhalation and ingestion, and the compound is presumably a moderate skin penetrant as well. Since methylethylketone is both water and lipid soluble, it is rather

evenly distributed in tissues.
[Zenz, C., O.B. Dickerson, E.P. Horvath. Occupational Medicine. 3rd ed. St. Louis, MO., 1994 149]**PEER REVIEWED**

Biological Half-Life:

Guinea pigs were given a single dose of **methyl ethyl ketone (**MEK) ip at 450 mg/kg. Blood samples were taken via cardiac puncture at 1, 2, 4, 6, 8, 12 and 16 hr after dosing. Serum half-life of MEK was estimated at 270 minutes.
[Divincenzo GD et al; Toxicol Appl Pharm 36: 511-22 (1976)]**PEER REVIEWED**

... The biological half lives for elimination of acetone and MEK calculated on the basis of a first order kinetic assumption were 3.9 hours and 49 minutes, respectively. ... Workers exposed to acetone or MEK for 6 to 8 hours could expect to have a residual body burden of acetone the next morning, whereas MEK would be essentially eliminated.
[Brown WD et al; The Changing Nature of Work and Workforce, Proceedings of the Third Joint US-Finish Science Symposium p.111-14 (1986)]**PEER REVIEWED**

The distribution of MEK in human tissues was examined ... in two solvent-exposed workers who died suddenly of heart attacks at the workplace. ... Distribution volumes were 6.0 for vessel-rich tissues, 39.6 for muscle and 12.8 for fat. Biological half-lives for the same tissues were 0.8, 21.8 and 23.3 min, respectively.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.51 (1993)]**PEER REVIEWED**

Both animal and human data indicate a rapid turnover of MEK. In guinea-pigs receiving an ip dose of 450 mg MEK/kg, the half-life of MEK in blood serum was 4.5 hr and the clearance time for MEK in serum was 12 hr. For the metabolites 2-butanol, 3-hydroxy-2-**butanone** and 2,3-butanediol, the clearance time in serum was 11 hr ... In a study ... on rats given an oral dose of 2-**butanone** of 2.1 mg/kg, there was a half-life of 3.6 hr for MEK in blood if the rate of loss was assumed to be constant between the two times of measurement (4 and 18 hrs) after dosing. Data from a study ... on rats receiving oral doses of 2-butanol or MEK also indicate a half-life of about 4 hr for MEK. ... the clearance rate for 3-hydroxy-2-**butanone** and 2,3-butanediol was independent of dose for the two doses used (0.4 and 0.8 g/kg) and that the half-lives for these metabolites of MEK were 47 min and 3.45 hr, respectively.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.56 (1993)]**PEER REVIEWED**

... reported a steady incr in blood concn during 4-hr exposures of human volunteer subjects to 590 mg/cu m (200 ppm) and observed a rapid elimination of MEK, with half-lives of 30 min during the first post-exposure hr and 81 min thereafter. An inhalation study with two volunteer subjects exposed to MEK for 4 hr at concn of 74,590 and 1,180 mg/cu m (25,200 and 400 ppm, respectively) indicated that the kinetics of MEK were dose dependent at higher exposure concn, i.e., much higher levels of MEK in blood were reached relative to inhaled concn, and the post-exposure elimination of MEK in blood was slower (zero-order kinetics). Simulated exposure to MEK for 8 hr suggests that saturation kinetics are reached at about 295 mg/cu m (100 ppm) at rest and 148 mg/cu m (50 ppm) during light exercise ... .
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.56

(1993)]**PEER REVIEWED**

Mechanism of Action:

The effects of the solvents n-hexane, **butanone** (**methyl ethyl ketone,** MEK) and a mixture of both in the intrapulmonary nerve system of rats were studied by light and electron microscopy. The alteration in the fine structures of the tissue consisted in a disseminated swelling of axons due to a striking multiplication of neurofilaments. Nonspecific axonal alterations could be demonstrated as well. The latter consisted in clusters of phospholipid material within the axoplasm of nerve fibers and the cytoplasm of Schwann cells plus an accumulation of glycogen granules in the axoplasm. Additionally, single degenerative changes of Schwann cells were observed. An enzyme associated metabolic damage with a concomitant impairment of axonal flow is discussed as a possible underlying pathomechanism.
[Schmidt R et al; Respiration 46 (4): 362-9 (1984)]**PEER REVIEWED**

There is very limited info on the mechanisms of toxic action of MEK. Relatively high inhaled concn 1,475-29,500 mg/cu m (500-10,000 ppm) caused pulmonary vasoconstriction and hypertension in cats and dogs ... From the toxicological point of view, interactions leading to the potentiation of effects, particularly neurotoxicity, by other intrinsically toxic substances constitute the main hazard of MEK. The mechanisms underlying these interactions are incompletely known ... .
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.57 (1993)]**PEER REVIEWED**

Interactions:

IT DOES NOT APPEAR TO BE NEUROTOXIC BY ITSELF, IT POTENTIATES NEUROTOXICITY OF OTHER HEXACARBONS; REPORTED IN HUMANS EXPOSED TO **METHYL ETHYL KETONE (**MEK) & N-HEXANE.
[ALTENKIRCH ET AL; J NEUROL 214: 152 (1977)]**PEER REVIEWED**

Methyl ethyl ketone potentiates carbon tetrachloride hepatoxicity in rats. Oral dosing with **methyl ethyl ketone** at 1.87, 2.4, or 1.2 ml/kg followed by ip injection with carbon tetrachloride at 0.1 ml/kg significantly enhanced the hepatotoxicity of carbon tetrachloride as measured by increased serum glutamic pyruvic transaminase activity and hepatic triglyceride concentration and decreased hepatic glucose-6-phosphatase activity.
[Traiger GJ, Bruckner JV; J Pharmacol Exp Ther 196: 493 (1976)]**PEER REVIEWED**

A study of the potential relationship between **methyl ethyl ketone** and 2,5-hexanedione was conducted. Male F344 rats weighing between 200 and 320 g were used. A sensorimotor/behavioral battery consisting of two simple reflex tests, hind limb grasp and hind limb place, and two complex function tests, balance beam and accelerating rotorod performance, was used for identification and quantification of neurological deficits. ... The enhancement of 2,5-hexanedione induced toxicity by **methyl ethyl ketone** could be correlated with higher tissue exposures of 2,5-hexanedione in animals receiving the combined treatment. ... **Methyl ethyl ketone** may compete with 2,5-hexanedione for critical and non-critical binding sites at the target neurofilament proteins.
[Ralston WH et al; Toxicol Appl Pharm 81 (2): 319-27 (1985)]**PEER REVIEWED**

The effects of acute exposure to toluene and **methyl ethyl ketone (**MEK) singly and in combination

were investigated. ... The effects of these chemicals on behavior and body burden were determined. ... MEK had no effect on any measures. Behavior performance was not affected by the combination of toluene and MEK. Body burden of the two solvents was not additive. ... Neither chemical potentiated the effect of the other at the concentrations studied.
[Dick RB et al; Int Arch Occup Environ Health 54 (2): 91-109 (1984)]**PEER REVIEWED**

... An important observation was the marked potentiation of peripheral neurotoxicity observed when animals were exposed to n-butyl ketone in combination with **methyl ethyl ketone** at a ratio of 1:5, n-butyl ketone: **methyl ethyl ketone.** The latter solvent showed no neurotoxic effect alone.
[Saida K et al; J Neuropathol Exp Neurol 35 (3): 207-25 (1976)]**PEER REVIEWED**

... The toxic neuropathy induced by **methyl ethyl ketone** is clinically and morphologically identical with that induced by n-hexane and methyl butyl ketone. **Methyl ethyl ketone** can act synergistically with n-hexane to produce toxic neuropathy.
[Alterkirch H et al; J Neurology 214: 137-52 (1977)]**PEER REVIEWED**

Ingestion of ethanol (0.8 g/kg) combined with an inhalation exposure to MEK (590 mg/cu m, 200 ppm) inhibited the oxidative metabolism of MEK and led to a marked incr in the blood concn of MEK ... There was a concurrent, even more pronounced elevation of the blood 2-butanol concn; the most likely explanation is competitive inhibition by ethanol of the oxidation of 2-butanol back to MEK. Ethanol also appeared to interact with the further biotransformation of 2,3-butanediol as the urinary excretion of the metabolite was incr. Co-exposure with xylene, however, had no effect on the human metabolism or rate of elimination of MEK ... .
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.57 (1993)]**PEER REVIEWED**

... found that MEK and certain other polar aprotic solvents were strong inducers of aneuploidy in the yeast. The induction of aneuploidy by MEK was markedly potentiated by coexposure to ethyl acetate ... or with nocodazol ... .
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.80 (1993)]**PEER REVIEWED**

MEK interacts with hexacarbon compounds and potentiates their neurotoxicity ... Potentially MEK co-exposure could affect the metabolism of the hexacarbon compounds or the toxic process by which the hexacarbons induce the neuropathy. ... The metabolic pathway involves hepatic microsomal oxidation to 2,5-hexanedione, the proximate neurotoxicant, which is thought to induce cross-linking of neurofilaments, blockage of transport at the node of Ranvier, and swelling from accumulated neurofilaments proximal to the nodes and axonal degeneration distal to the nodes.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.101 (1993)]**PEER REVIEWED**

Carbon tetrachloride (CCl4), chloroform (CHCl3) and related haloalkane solvents are liver and kidney poisons as well as central nervous depressants ... It has long been known that the hepatotoxic action of CCl4 is potentiated by ethanol, and more recently that the hepatic and/or renal toxicity of CCl4, CHCl3, trichloroethylene, 1,1,2-trichloroethane and related compounds is potentiated by n-hexane, ethanol, isopropanol, acetone, MEK, MBK, 2,5-HD, and other ketones or chemicals that are metabolized to

ketones ... Even an incr of naturally occurring ketones in the body via diabetes can precipitate potentiation. Decr the transformation of isopropanol to acetone by the admin of an inhibitor of alcohol dehydrogenase, pyrazole, has reduced potentiation of haloalkane toxicity. Although the phenomenon is referred to as haloalkane toxicity, experimental work in general appears largely or entirely limited to chlorinated compounds, and specific studies on MEK are limited to interactions with CCl4 and CHCl3.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.115 (1993)]**PEER REVIEWED**

Pharmacology:

Interactions:

IT DOES NOT APPEAR TO BE NEUROTOXIC BY ITSELF, IT POTENTIATES NEUROTOXICITY OF OTHER HEXACARBONS; REPORTED IN HUMANS EXPOSED TO **METHYL ETHYL KETONE (**MEK) & N-HEXANE.
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[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.115 (1993)]**PEER REVIEWED**

Environmental Fate & Exposure:

Environmental Fate/Exposure Summary:

Methyl ethyl ketone's production and use as a solvent for coatings, resins, rubbers, plastics, pharmaceuticals, adhesives and rubber cements will result in its release to the environment through various waste streams. Its use as a starting material or intermediate in the manufacture of chemical products will also lead to its release to the environment. **Methyl ethyl ketone** occurs naturally as a metabolic byproduct of plants and animals and is released into the atmosphere by volcanoes and forest fires. Based on an experimental vapor pressure of 91 mm Hg at 25 deg C, **methyl ethyl ketone** is expected to exist solely as a vapor in the ambient atmosphere. Vapor-phase **methyl ethyl ketone** is degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals with an estimated atmospheric half-life of about 14 days. This compound is also expected to undergo photolysis in the atmosphere by natural sunlight. Photochemical degradation of **methyl ethyl ketone** by natural sunlight is expected to occur at approximately 1/5 the rate of degradation by photochemically produced hydroxy radicals. **Methyl ethyl ketone** is expected to have very high mobility in soils based upon measured Koc values of 29 and 34 obtained in silt loams. Volatilization from dry soil surfaces is expected based upon the vapor pressure of this compound. Volatilization from moist soil surfaces is also expected based upon the measured Henry's Law constant of 4.7X10-5 atm-cu m/mol. The volatilization half-life of **methyl ethyl ketone** from silt and sandy loams was measured as 4.9 days. This compound is expected to biodegrade under aerobic and anaerobic conditions. In water, **methyl ethyl ketone** is not expected to adsorb to suspended solids or sediment based upon its measured Koc values. Volatilization from water surfaces is expected to be an important environmental fate process given its Henry's Law constant. Estimated half-lives for a model river and model lake are 19 and 197 hours, respectively. Bioconcentration in aquatic organisms is considered low based upon an estimated BCF value of 1. Occupational exposure may be through inhalation and dermal contact with this compound at workplaces where **methyl ethyl ketone** is produced or used. The general population may be exposed to **methyl ethyl ketone** through the use of commercially available products containing this compound such as paints, adhesives, and rubber cements. Exposure will also arise from inhalation of ambient air and ingestion of drinking water and food that contains **methyl ethyl ketone. (**SRC)
PEER REVIEWED

Probable Routes of Human Exposure:

NIOSH has est worker exposure to **methyl ethyl ketone** at 3,031,000 ...
[Sittig, M. Handbook of Toxic and Hazardous Chemicals and Carcinogens, 1985. 2nd ed. Park Ridge, NJ: Noyes Data Corporation, 1985. 601]**PEER REVIEWED**

Artificial leather workers /are at risk of exposure/.
[Arena, J.M. and Drew, R.H. (eds.) Poisoning-Toxicology, Symptoms, Treatments. 5th ed. Springfield, IL: Charles C. Thomas Publisher, 1986. 358]**PEER REVIEWED**

NIOSH (NOES Survey 1981-1983) has statistically estimated that 1,221,857 workers (201,308 of these are female) are potentially exposed to **methyl ethyl ketone** in the US(1). Occupational exposure may be through inhalation and dermal contact with this compound at workplaces where **methyl ethyl ketone** is produced or used(SRC). The 8 hour TWA exposure to **methyl ethyl ketone** was 45.4 ppm in a survey of 50 occupationally exposed male subjects working in a magnetic videotape producing factory(2). These workers had average concns of **methyl ethyl ketone** of 2 ppm and 1.4 mg/l in breath and blood samples respectively(2). The mean concn of **methyl ethyl ketone** in the breathing zones of 47 US plants using

polyurethane coatings was 4.33 ppm(3). **Methyl ethyl ketone** was detected in the breathing zones in 20 of 70 samples (mean concn 12 mg/cu m) obtained from autobody shops and spray paint shops in Australia(4).
[(1) NIOSH; National Occupational Exposure Survey (NOES) (1983) (2) Sia Gl et al; Environ Monit Assess 19: 401-11 (1991) (3) Myer HE et al; Am Ind Hyg Assoc J 54: 663-70 (1993) (4) Winder C, Turner PJ; Ann Occup Hyg 36: 385-94 (1992)]**PEER REVIEWED**

The general population may be exposed to **methyl ethyl ketone** through the use of commercially available products containing this compound such as paints, adhesives, and rubber cements(SRC). Exposure will also arise from inhalation of ambient air, ingestion of drinking water and food that contains **methyl ethyl ketone(**SRC). The average blood concn of **methyl ethyl ketone** in 600 non-occupationally exposed individuals in the US was 7.1 ppb(1).
[(1) Ashley DL et al; Clin Chem 40: 1401-04 (1994)]**PEER REVIEWED**

Body Burden:

Detected in 5 of 8 samples of mother's milk from 4 USA urban areas.
[(1) Pellizzari ED et al; Bull Environ Contam Toxicol 28: 322-8 (1982)]**PEER REVIEWED**

The kinetics of inhaled **methyl ethyl ketone (**MEK) in human volunteers was studied in an exposure chamber. Relative pulmonary uptake was about 53% throughout a 4 hr exposure period at 200 ppm. Blood MEK concentration rose steadily until the end of exposure. Repeated bicycle exercise increased the overall blood MEK level markedly in comparison to sedentary activity, with transient peaks in association with cycling; thus blood MEK concentration depended both on the rate of uptake and the amount taken up. Only 3% of the absorbed dose was excreted unchanged by exhalation. A well known metabolite of MEK, 2,3-butanediol, was detected in the urine with maximum rates of excretion at about 6 to 12 hr from the beginning of exposure. About 2% of the MEK dose taken up by the lungs was excreted in the urine as 2,3-butanediol. ... Elimination of MEK in blood appeared to exhibit two phases: the initial alpha-phase (T1/2= 30 min; kel alpha= 0.023) over the first post-exposure hour, followed by the terminal beta-phase (T1/2= 81 min; kel beta= 0.009).
[Liira J et al; Int Arch Occup Environ Health 60 (3): 195-200 (1988)]**PEER REVIEWED**

Worker exposures were investigated in April 1983 at the Hoover Company, North Canton, Ohio. ... Area and personal air samples for numerous contaminants were collected and nonionizing radiation levels were measured. ... General medical questionnaires and blood tests for **methyl ethyl ketone (**MEK) were given to exposed workers. ... No respiratory symptoms or pulmonary function disorders were identified in the foundry workers, and MEK was detected in the blood of only one worker at 1.4 ug/ml. ...
[NIOSH; Health Hazard Evaluation Report No. HETA-82-280-1407 (1984)]**PEER REVIEWED**

Natural Pollution Sources:

Methyl ethyl ketone occurs naturally as a metabolic byproduct of plants and animals and is released into the atmosphere by volcanoes and forest fires(1).
[(1) Graedel TE et al; Atmospheric Chemical Compounds. NY,NY: Academic

Press p. 263 (1986)]**PEER REVIEWED**

Artificial Pollution Sources:

Methyl ethyl ketone's production and use as a solvent for coatings, resins, rubbers, plastics, pharmaceuticals, adhesives and rubber cements(1-3) will result in its release to the environment through various waste streams(SRC). Its use as a starting material or intermediate in the manufacture of chemical products(2,3) will also lead to its release to the environment(SRC).
[(1) Budvari S; Merck Index, 12th ed, Whitehouse Station,NJ: Merck & Co. p. 1773 (1996) (2) Browning E; Toxicity and Metabolism of Industrial Solvents. NY,NY: American Elsevier (1965) (3) Lewis RJ Sr ed; Hawley's Condensed Chemical Dictionary. 12th ed NY,NY: Van Nostrand Rheinhold Co p. 768 (1993)]**PEER REVIEWED**

Water pollution: Polyvinyl chloride pipe cement used for joint connection caused 4.5 ppm, 6 months after polyvinyl chloride pipe installation and 2.2 ppm after 8 months (at equilibrium condition-reached in about 48 hr).
[Verschueren, K. Handbook of Environmental Data of Organic Chemicals. 2nd ed. New York, NY: Van Nostrand Reinhold Co., 1983. 851]**PEER REVIEWED**

Environmental Fate:

TERRESTRIAL FATE: Measured Koc values of 29 and 34 were obtained for **methyl ethyl ketone** in silt loams(1). Based on a recommended classification scheme(2), **methyl ethyl ketone** is expected to have very high mobility in soil(SRC). Volatilization of **methyl ethyl ketone** from dry soil surfaces is expected based upon an experimental vapor pressure of 91 mm Hg at 25 deg C(3). Volatilization from moist soil surfaces(SRC) is also expected given the measured Henry's Law constant of 4.7X10-5 atm-cu m/mole(4). The volatilization half-life of **methyl ethyl ketone** from silt and sandy loams was measured as 4.9 days(5). **Methyl ethyl ketone** is expected to biodegrade under both aerobic and anaerobic conditions as indicated by numerous screening tests(6-9).
[(1) Walton BT et al; J Environ Qual 21: 552-58 (1992) (2) Swann RL et al; Res Rev 85: 23 (1983) (3) Alarie Y et al; Toxicol Appl Pharmacol 134: 92-99 (1995) (4) Bhattacharaya SK et al; Water Res 30: 3099-3105 (1996) (5) Anderson TA et al; J Environ Qual 20: 420-24 (1991) (6) Bridie Al, et al; Water Res 13: 627-30 (1979) (7) Price KS et al; J Water Pollut Control Fed 46: 63-77 (1974) (8) Bhattacharaya SK et al; Wat Res 30: 3099-3105 (1996) (9) Suflita JM, Mormile MR; Environ Sci Technol 27: 976-78 (1993)]**PEER REVIEWED**

AQUATIC FATE: Based on experimental Koc values of 29 and 34 obtained in silt loams(1), and a recommended classification scheme(2), **methyl ethyl ketone** is not expected to adsorb to suspended solids and sediment in water(SRC). **Methyl ethyl ketone** is expected to volatilize from water surfaces(3,SRC) based on the measured Henry's Law constant of 4.7X10-5 atm-cu m/mole(4). Estimated half-lives for a model river and model lake are 19 and 197, hours respectively(3,SRC). Biodegradation of this compound is expected based upon numerous screening tests(5-8). According to a classification scheme(9), an estimated BCF value of 1(3,SRC), from an experimental log Kow of 0.29(10,SRC), suggests that bioconcentration in aquatic organisms is low(SRC).

[(1) Walton BT et al; J Environ Qual 21: 552-58 (1992) (2) Swann RL et al; Res Rev 85: 23 (1983) (3) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington DC: Amer Chem Soc pp. 4-9 (1990) (4) Bhattacharaya SK et al; Water Res 30: 3099-3105 (1996) (5) Bridie Al, et al; Water Res 13: 627-30 (1979) (6) Price KS et al; J Water Pollut Control Fed 46: 63-77 (1974) (7) Bhattacharaya SK et al; Wat Res 30: 3099-3105 (1996) (8) Suflita JM, Mormile MR; Environ Sci Technol 27: 976-78 (1993) (9) Franke C et al; Chemosphere 29: 1501-14 (1994) (10) Hansch C et al; Exploring QSAR Hydrophobic, Electronic and Stearic Constants Washington,DC: Amer Chem Soc (1995)]**PEER REVIEWED**

ATMOSPHERIC FATE: According to a model of gas/particle partitioning of semivolatile organic compounds in the atmosphere(1), **methyl ethyl ketone,** which has an experimental vapor pressure of 91 mm Hg at 25 deg C(2), will exist solely as a vapor in the ambient atmosphere. Vapor-phase **methyl ethyl ketone** is degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals(SRC); the half-life for this reaction in air is estimated to be about 14(3,SRC) days. **Methyl ethyl ketone** is also expected to undergo photodecomposition in the atmosphere by natural sunlight(4,5). Photochemical degradation of **methyl ethyl ketone** by natural sunlight is expected to occur at approximately 1/5 the rate of degradation by photochemically produced hydroxyl radicals(5).
[(1) Bidleman TF; Environ Sci Technol 22: 361-367 (1988) (2) Alarie Y et al; Toxicol Appl Pharmacol 134: 92-99 (1995) (3) Atkinson R; J Phys Chem Ref Data (1989) (4) Raber W et al; pp. 364-70 in Phys Chem Behav Atmos Pollut 5th ed Restelli G, Angeletti G eds, Kluwer: Dordecht, Netherlands (1990) (5) Altshuller AP; J Atmos Chem 13: 155-82 (1991)]**PEER REVIEWED**

Environmental Biodegradation:

Methyl ethyl ketone (MEK) is readily oxidized by microorganisms in activated sludge following selection and/or adaptation, with over 80% being removed in 24 hr. Metabolism in unacclimated sludges is slow.
[USEPA; Methyl Ethyl Ketone III: Exposure Aspects USEPA Contract No. 68-01-6147 (1981)]**PEER REVIEWED**

Biological oxygen demand (BOD) after 5 days @ 20 deg C: 1.515-1.92; 2.24 (std dilution technique, normal sewage seed); 5.3 (Dutch std test method); 1.81 (@ 10 mg/l, unadapted sewage, 1 days lag period).
[Verschueren, K. Handbook of Environmental Data of Organic Chemicals. 2nd ed. New York, NY: Van Nostrand Reinhold Co., 1983. 851]**PEER REVIEWED**

Chemical oxygen demand (COD): 2.20-2.31; 5.3 (Dutch std test method); theoretical oxygen demand (ThOD): 2.44; permanganate test value: 0.29.
[Verschueren, K. Handbook of Environmental Data of Organic Chemicals. 2nd ed. New York, NY: Van Nostrand Reinhold Co., 1983. 851]**PEER REVIEWED**

Using standard BOD and COD dilution techniques and a sewage inoculum, a theoretical BOD of 83% and a theoretical COD of 95% was reported over a 5 day incubation period(1). The percent theoretical BOD of **methyl ethyl ketone** in freshwater was reported as 76%, 82%, 84% and 89% over 5, 10 15 and 20 day incubation periods respectively(2). The percent theoretical BOD of **methyl ethyl ketone** in synthetic saltwater was reported as 32%, 62%, 63% and 69% over 5, 10 15 and 20 day incubation periods respectively(2). 92-95% biodegradation was reported when 0.25 mg/l of **methyl ethyl ketone** was fed through an activated sludge from a wastewater treatment plant over a 3 week incubation period(3). The percent theoretical methane recovery of **methyl ethyl ketone** in an anaerobic aquifer was 89% over a 3 week incubation period following a 15 day acclimation period(4).
[(1) Bridie Al, et al; Water Res 13: 627-30 (1979) (2) Price KS et al; J Water Pollut Control Fed 46: 63-77 (1974) (3) Bhattacharaya SK et al; Wat Res 30: 3099-3105 (1996) (4) Suflita JM, Mormile MR; Environ Sci Technol 27: 976-78 (1993)]**PEER REVIEWED**

Environmental Abiotic Degradation:

The rate constant for the vapor-phase reaction of **methyl ethyl ketone** with photochemically-produced hydroxyl radicals has been measured as 1.15X10-12 cu cm/molecule-sec at 25 deg C(1). This corresponds to an atmospheric half-life of about 14 days at an atmospheric concn of 5.0X10+5 hydroxyl radicals per cu cm(1,SRC). **Methyl ethyl ketone** is also expected to undergo photodecomposition in the atmosphere by natural sunlight(2,3). Based on the actinic fluxes within the planet boundary layer, along with an estimated quantum yield and absorption cross section, the rate of photodissociation of **methyl ethyl ketone** by natural sunlight is approximately 1/5 the rate of dissociation by hydroxyl radicals(3). This compound is not expected to undergo hydrolysis in the environment due to a lack of functional groups which hydrolyze(SRC).
[(1) Atkinson R; J Phys Chem Ref Data (1989) (2) Raber W et al; pp. 364-70 in Phys Chem Behav Atmos Pollut 5th ed Restelli G, Angeletti G eds, Kluwer: Dordecht, Netherlands (1990) (3) Altshuller AP; J Atmos Chem 13: 155-82 (1991)]**PEER REVIEWED**

Environmental Bioconcentration:

An estimated BCF value of 1 was calculated for **methyl ethyl ketone(**SRC), using an experimental log Kow of 0.29(1) and a recommended regression-derived equation(2). According to a classification scheme(3), this BCF value suggests that bioconcentration in aquatic organisms is low(SRC).
[(1) Hansch C et al; Exploring QSAR Hydrophobic, Electronic and Stearic Constants Washington DC: Amer Chem Soc (1995) (2) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington DC: Amer Chem Soc pp. 5-4, 5-10 (1990) (3) Franke C et al; Chemosphere 29: 1501-14 (1994)]**PEER REVIEWED**

Soil Adsorption/Mobility:

Measured Koc values of 29 and 34 were obtained for **methyl ethyl ketone** in silt loams(1). Based on a recommended classification scheme(2), **methyl ethyl ketone** is expected to have very high mobility in soil(SRC).
[(1) Walton BT et al; J Environ Qual 21: 552-58 (1992) (2) Swann RL et al; Res Rev 85: 23 (1983)]**PEER REVIEWED**

Volatilization from Water/Soil:

The Henry's Law constant for **methyl ethyl ketone** was measured as 4.7X10-5 atm-cu m/mole(SRC) at 25 deg C(1). This value indicates that **methyl ethyl ketone** will volatilize from water surfaces(2,SRC). Based on this Henry's Law constant, the volatilization half-life from a model river (1 m deep, flowing 1 m/sec, wind velocity of 3 m/sec) is estimated as approximately 19 hours(2,SRC). The volatilization half-life from a model lake (1 m deep, flowing 0.05 m/sec, wind velocity of 0.5 m/sec) is estimated as approximately 197 hours(2,SRC). **Methyl ethyl ketone** is expected to volatilize from dry soil surfaces given its experimental vapor pressure of 91 mm Hg at 25 deg C(3,SRC). The volatilization half-life of **methyl ethyl ketone** from silt and sandy loams was measured as 4.9 days(4).
[(1) Bhattacharaya SK et al; Water Res 30: 3099-3105 (1996) (2) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington DC: Amer Chem Soc pp. 15-1 to 15-29 (1990) (3) Alarie Y et al; Toxicol Appl Pharmacol 134: 92-99 (1995) (4) Anderson TA et al; J Environ Qual 20: 420-24 (1991)]**PEER REVIEWED**

Environmental Water Concentrations:

DRINKING WATER: A Federal survey of public groundwater supplies detected **methyl ethyl ketone** in less than 5% of the samples(1). **Methyl ethyl ketone** was identified, not quantified, in drinking water supplies from 7 cities from varied sources and with different types of pollutant sources(2-4).
[(1) Dyksen JE, Hess AF III; J Amer Water Works Assoc 74: 394-403 (1982) (2) Coleman WE et al; pp. 305-207 in Analysis and Identification of Organic Substances in Water. Keith L ed Ann Arbor, MI Ann Arbor Press (1976) (3) Scheeman MA et al; Biomed Mass Spectrom 4: 209-11 (1974) (4) USEPA; New Orleans Area Water Supply Study. Draft Analytical Report by the Lower Mississippi River Facility, Slidell (1974)]**PEER REVIEWED**

GROUNDWATER: **Methyl ethyl ketone** was detected in groundwater at a coal strip-mine in Ohio at a concn of 650 mg/l(1). **Methyl ethyl ketone** was identified, not quantified, in on-site and off-site groundwater near a landfill in New Jersey(2). **Methyl ethyl ketone** was detected in the groundwater of a coal strip-mine in Lackawanne, PA at a maximum concn of 29,000 ppb(3). **Methyl ethyl ketone** was detected at an average concn of 12 ug/l in the groundwater of 19 solid waste disposal facilities in Wisconsin(4) and in the range of 0-91 ug/l in the groundwater of a landfill located in New Castle, DE(5). **Methyl ethyl ketone** was detected at an average concn of 60 ug/l in the groundwater of a chemical manufacturing facility in Alabama(6).
[(1) USEPA; Superfund Record of Decision : Summit National Site, Deerfield OH. USEPA/ROD/R85-88/068 (1988) (2) USEPA; Superfund Record of Decision: Lipari Landfill Mantau Township, NJ. USEPA/ROD/RO2-88/074 (1988) (3) ATSDR; Health assessment for Beacon Heights Landfill National Priorities List (NPL) Site, Beacon Falls, Connecticut, Region 1. CERCLIS NO. CTD001145671. Agency for Toxic Substances and Disease Registry PB90-135971 (1990) (4) Battista JR, Connelly JP; VOC contamination at selected Wisconsin landfills - sampling results and policy implications. Wisc Dept of Natural Resources, Madison, WI. Publ-SW-094 (1989) (5) ATSDR; Health assessment for Tybouts Corner

land (Tybouts) National Priorities List (NPL) site, Wilmington, New Castle County, Deleware, Region 3. CERCLIS NO. DED000606079. Agency for Toxic Substances and Disease Registry PB90-144387 (1989) (6) USEPA; Superfund Record of Decision: Ciba-Geigy (Mcintosh Plant), AL. USEPA/ROD/R04-89/056 (1989)]**PEER REVIEWED**

SURFACE WATER: **Methyl ethyl ketone** was identified, not quantified, in the Black River in Tuscaloosa, AL(1) and Newark Bay, NJ(2). **Methyl ethyl ketone** was detected in the Potomac River at a concn of less than 40 ug/l(3). **Methyl ethyl ketone** was detected in a creek in New Castle, DE near a landfill at concns of 0-11,000 ug/l(4).
[(1) Berstch W et al; J Chromatog 112: 701-18 (1975) (2) Gunster DG et al; Environ Pollut 82: 245-53 (1993) (3) Hall LWJR et al; Aquat Toxicol 10: 73-99 (1987) (4) ATSDR; Health assessment for Tybouts Corner land (Tybouts) National Priorities List (NPL) site, Wilmington, New Castle County, Deleware, Region 3. Agency for Toxic Substances and Disease Registry PB90-144387 (1989)]**PEER REVIEWED**

RAIN/SNOW: An unspecified concn of **methyl ethyl ketone** was detected in the rainfall in Japan(1). **Methyl ethyl ketone** was detected at concns of 0-0.47 ppb in the clouds in California and as trace amounts in fog-ice(2). **Methyl ethyl ketone** was detected in clouds (1,390 ng/l) and rainfall (139 ng/l) at a state park in North Carolina(3).
[(1) Kato T et al; Yokohama Kokuritsu Daigaku Kankyo Kagaku Kenkyu Senta Kiyo 6: 11-20 (1980) (2) Grosjean D, Wright B; Atmos Environ 17: 2093-6 (1983) (3) Aneja VP et al; J Air Waste Manage Assoc 43: 1239-44 (1993)]**PEER REVIEWED**

Effluent Concentrations:

Methyl ethyl ketone was detected in the leachate of several municipal landfills at concns between 110-6,600 ug/l(1). **Methyl ethyl ketone** was detected in the leachate of a sand and gravel pit near Utica, NY at a concn of 540 ug/l(2). **Methyl ethyl ketone** was detected in the leachate of an industrial landfill (53 mg/l) and a municipal landfill (0.11-27 mg/l)(3).
[(1) Christensen TH et al; Crit Rev Environ Sci Technol 24: 119-202 (1994) (2) USEPA; Superfund Record of Decision: Ludlow Sand and Gravel Site, Town of Paris Oneida County, NY USEPA/ROD/R02-88/067 (1988) (3) Brown KW, Donnelly KC; Haz Waste Haz Mater 5: 1-30 (1988)]**PEER REVIEWED**

Methyl ethyl ketone was detected in the effluent of a municipal landfill in Quebec, Ontario at concns of 5,200 ppb and 3092 ppb(1). **Methyl ethyl ketone** was identified, not quantified in the emissions of a waste incinerator in West Germany(2), automobiles(3) and common household waste(4-7). **Methyl ethyl ketone** was detected in the effluent from a solid waste composting plant at concns of 130 ug/cu m (background air), 25,500 ug/cu m(tipping area), 1,400 ug/cu m (shredder), 9,400 ug/cu m(indoor air), 36,000 ug/cu m (digester), 4,300 ug/cu m(fresh compost), 8,700 ug/cu m(middle age compost), 14,500 ug/cu m(old compost) and 1,400 ug/cu m(curing region)(8). **Methyl ethyl ketone** was identified, not quantified, in the emissions of 200 out of 1,026 common household products(9). **Methyl ethyl ketone** was detected in the emissions of a photocopying machine at rates of less than 100 ug/hr to 380 ug/hr(10).

Methyl ethyl ketone was detected at a concn of 974 ug/cu m in the emissions of active compost at a composting facility in Virginia(11).
[(1) Brosseau, Heitz M; Atmos Environ 25A: 1473-77 (1994) (2) Jay K, Stieglitz L; Chemosphere 30: 1249-60 (1995) (3) Harley RA et al; Environ Sci Technol 26: 2395-2408 (1992) (4) Wilkins CK, Larsen K; J High Resol Chromatogr 18: 373-77 (1995) (5) Wilkins K, Larsen K; Chemosphere 31: 3225-36 (1995) (6) Wilkins K, Larsen K; Chemosphere 32: 2049-55 (1996) (7) Wilkins K; Chemosphere 29: 47-53 (1994) (8) Eitzer BD; Environ Sci Technol 29: 896-902 (1995) (9) Sack TM et al; Atmos Environ 26A: 1063-70 (1992)(10) Leovic KW et al; J Air Waste Manage Assoc 46: 821-29 (1996) (11) Vandurme GP et al; Water Environ Res 64: 19-27 (1992)]**PEER REVIEWED**

Sediment/Soil Concentrations:

Methyl ethyl ketone was detected in the soil of a coal strip mine in Ohio at mean concns of 1,682 ug/kg (surface soil), 11,750 ug/kg (2-4 feet), 38,000 ug/kg (4-6 feet), 5,368 ug/kg (6-8 feet)(1). **Methyl ethyl ketone** was identified, not quantified, in the subsurface soil of a gravel mine in Tennessee(2). **Methyl ethyl ketone** was detected at an average concn of 1,615 ug/kg in the soil of an unauthorized hazardous waste disposal facility in New Jersey(3). **Methyl ethyl ketone** was detected at an average concn of 32 ug/kg in the soil of a waste disposal facility in Kansas(4).
[(1) USEPA; Superfund Record of Decision: Summit National Site, Deerfield OH. USEPA/ROD/R85-88/068 (1988) (2) USEPA; Superfund Record of Decision: Galloway Ponds Site, Galloway, TN. USEPA/ROD/R04-86/013 (1987) (3) USEPA; Superfund Record of Decision: Lang Property Pemberton Township, NJ USEPA/ROD/R02-86/031 (1987) (4) USEPA; Superfund Record of Decision: Doepke Disposal (Holliday), KS USEPA/ROD/R07-89/032 (1989)]**PEER REVIEWED**

Atmospheric Concentrations:

The presence of solvents such as toluene, xylene, **methyl ethyl ketone,** and other similar products in the indoor air of an automobile body repair shop, an offset printing facility and the adjacent dwellings was monitored, and the individual exposure of the corresponding workers and residents was tested by biological monitoring of exhaled breath and by personal air sampling. The concentrations of solvents tested in the air of both sites surveyed were lower than prevailing Dutch Maximum Allowable Concentration levels. The levels of solvents recorded in the air of apartments situated on top of the facilities surveyed were significantly higher than the levels recorded in the surrounding dwellings. The levels of **methyl ethyl ketone,** toluene and xylene in personal air samples of employees at the body shop were 1.5 times higher than in ambient air. The level of toluene in alveolar air of residents living above the automobile repair shop was 50 percent higher than that recorded in spot samples. The levels of other solvents were equal to or lower than the detection level. At the offset printing facility, toluene, xylene, butylacetate, 2-ethoxyethanol and cyclohexanone in air and in personal air samples followed the same general pattern identified for the body shop. In a dwelling next to the shop and in an apartment on top of the shop, the concentrations ranged from 3 to 9 percent and 14 to 19 percent, respectively, of the levels recorded inside the facility itself.
[Verhoeff AP et al; Int Arch Occup Environ Health 59 (2): 153-63

(1987)]**PEER REVIEWED**

URBAN/SUBURBAN: **Methyl ethyl ketone** was detected at a mean concn of 1.5 ppb in Boston, MA(1). **Methyl ethyl ketone** was detected at mean concns of 1.35 ppb in Boston, MA, and 5.1 ppb in Houston, TX(2). The average concn of **methyl ethyl ketone** at 25 urban locations in the US was 1.4 ug/cu m(3). **Methyl ethyl ketone** was detected at a mean concn of 1.67 ppb in Los Angeles, CA(4) and in the Caldecott Tunnel in San Francisco, CA at a concn of 1.67 mg/l(5). **Methyl ethyl ketone** was detected at average concns of 0.222-1.366 ppb in Grenoble, France(6). An average concn of 0.638 ppb of **methyl ethyl ketone** was obtained from 714 atmospheric samples in the US(7).
[(1) Reiss R et al; J Air Waste Manage Assoc 45: 811-22(1995) (2) Kelly TJ et al; Environ Sci Technol 27: 1146-53 (1993) (3) Kelly TJ et al; Ambient concn summaries for Clean Air Act. Title III. Hazardous Air Pollutants. USEPA Contract No 68-D80082 USEPA/600/R-94/090 (1993) (4) Grosjean E et al; Environ Sci Technol 30: 2687-2703 (1996) (5) Kirschstetter TW et al; Environ Sci Technol 30: 661-70 (1996) (6) Foster P et al; Pollut Atmos: 175-91 (1991) (7) Shah JJ, Heyerdahl EK; Environ Sci Technol 22: 1381-88 (1988)]**PEER REVIEWED**

RURAL/REMOTE: **Methyl ethyl ketone** was detected at an average concn of 2.40 ng/l in the air of a state park in North Carolina(1). **Methyl ethyl ketone** was detected at an average concn of 18 ug/cu m at rural locations in Canada(2) and concns of 1.8-3.3 ppb in a rural location in Louisiana(3).
[(1) Aneja VP et al; J Air Waste Manage Assoc 43: 1239-44 (1993) (2) Chan CC et al; J Air Waste Manage Assoc 40: 62-67 (1990) (3) Khalil MAK, Rasmussen RA; J Air Waste Manage Assoc 42: 810-13 (1992)]**PEER REVIEWED**

SOURCE AREAS: **Methyl ethyl ketone** was detected at a median concn of 64 parts per trillion and a range of 10-1,900 parts per trillion(1) in source dominated areas in New Jersey(1). **Methyl ethyl ketone** was detected at a concn of 94 ppm near a reclamation plant(2).
[(1) Brodzinsky R, Singh HB; Volatile Organic Chemicals in the Atmos SRI International Contract 68-02-3452 (1982) (2) Lande SS et al; Investigation of Selected Potential Environmental Contaminants: Ketonic Solvents 331 p USEPA 560/2-76-003 (1976)]**PEER REVIEWED**

INDOOR AIR: **Methyl ethyl ketone** was detected at an average concn of 17.8 ug/cu m at dwellings in Canada(1) and 2.4 ppb in buildings in Boston, MA(2). **Methyl ethyl ketone** was detected in 2 federal office buildings in Portland, OR at concns between 2.0 and 40.9 ug/cu m(3). Four indoor air samples in the US had average concns of MEK of 9.238 ppb(4).
[(1) Chan CC et al; J Air Waste Manage Assoc 40: 62-67 (1990) (2) Reiss R et al; J Air Waste Manage Assoc 45: 811-22 (1995) (3) Hodgeson AT et al; J Air Waste Manage Assoc 41: 1461-68 (1991) (4) Shah JJ, Heyerdahl EK; Environ Sci Technol 22: 1381-88 (1988)]**PEER REVIEWED**

Food Survey Values:

NON-ALCOHOLIC BEVERAGES 70 PPM; ICE CREAM, ICES, ETC 270 PPM; CANDY 100 PPM; BAKED GOODS 100 PPM
[Fenaroli's Handbook of Flavor Ingredients. Volume 2. Edited,

translated, and revised by T.E. Furia and N. Bellanca. 2nd ed. Cleveland: The Chemical Rubber Co., 1975. 59]**PEER REVIEWED**

Methyl ethyl ketone was detected in Swiss cheese (0.3 ppm) and cream (0.154-0.177 ppm)(1). **Methyl ethyl ketone** was identified, not quantified, in the volatiles of roasted barley, bread, honey, chicken, oranges, black tea, and rum(1), kiwi fruit(2), chickpea seeds(3), mutton, chicken and beef(4). **Methyl ethyl ketone** was detected at a concn of 1.83 ug/g in rotten mussels in Japan(5).
[(1) Lande SS et al; Investigation of Selected Potential Environmental Contaminants: Ketonic Solvents. 331 pp. USEPA 560/2-76-003 (1976) (2) Tatsuka K et al; J Food Sci 38: 2176-80 (1990) (3) Rembold H et al; J Agric Food Chem 37: 659-62 (1989) (4) Shahidi F et al; CRC Crit Rev Food Sci Nature 24: 141-243 (1986) (5) Yasuhara A; J Chromatogr 409: 251-58 (1987)]**PEER REVIEWED**

Plant Concentrations:

32 samples of southern pea seed, Vigna unguiculata, were analyzed for volatiles. **Methyl ethyl ketone (**MEK) was found in all samples and the mean concn was 151 + or - 80 ppb (74 to 390 ppb).
[Fisher GS et al; J Agric Food Chem 27: 7-11 (1979)]**PEER REVIEWED**

Methyl ethyl ketone is emitted from pencil cedar, Zeravshan juniper, European firs and Evergreen cyprus(1). **Methyl ethyl ketone** was detected in 32 of 32 samples of southern pea seeds at a mean concn of 151 ppb(2).
[(1) Singh HB, Zimmerman PB; Adv Environ Sci Technol 24: 177-235 (1992) (2) Fisher GS et al; J Agric Food Chem 27: 7-11 (1979)]**PEER REVIEWED**

Milk Concentrations:

Milk 0.077-0.079 ppm, milk fat 8 ppm(1).
[(1) Lande SS et al; Investigation of Selected Potential Environmental Contaminants: Ketonic Solvents p. 102 USEPA 560/2-76-003 (1976)]**PEER REVIEWED**

Methyl ethyl ketone was identified, not quantified in human milk samples in Bayonne, NJ(1) Pittsburgh, PA(1) Baton Rouge, LA(1) and Australia(2). **Methyl ethyl ketone** was identified, not quantified in 5 of 8 samples of human milk from 4 US urban areas(3).
[(1) Erickson MD et al; Acquisition and chemical analysis of mother's milk for selected toxic substances. USEPA-560/13-80-029. Washington, DC: USEPA Off Pestic Toxic Substances (1980) (2) Urbach G; J Chromatogr 404: 163-74 (1987) (3) Pellizzari ED et al; Bull Environ Contam Toxicol 28: 322-8 (1982)]**PEER REVIEWED**

Environmental Standards & Regulations:

FIFRA Requirements:

Unless designated as an active ingredient in accordance with paragraph (b) or (c) of this section, this substance, when used in antimicrobial products, is considered inert, having no independent pesticidal

activity. The percentage of such an ingredient shall be included on the label in the total percentage of inert ingredients.
[40 CFR 162.60 (7/1/88)]**PEER REVIEWED**

Methyl ethyl ketone is exempted from the requirement of a tolerance when used as a solvent, cosolvent in accordance with good agricultural practice as inert (or occasionally active) ingredients in pesticide formulations applied to growing crops only.
[40 CFR 180.1001(d) (7/1/96)]**PEER REVIEWED**

Acceptable Daily Intakes:

... An Acceptable Daily Intake (ADI), defined as the amount of a chemical to which humans can be exposed on a daily basis over an extended period of time (usually a lifetime) without suffering a deleterious effect, for **methyl ethyl ketone** is 3.2 mg/day for oral exposure. ...
[USEPA; Health and Environmental Effects Profile for Methyl Ethyl Ketone p.80 (1988) EPA/600/X-85/363]**PEER REVIEWED**

TSCA Requirements:

Pursuant to section 8(d) of TSCA, EPA promulgated a model Health and Safety Data Reporting Rule. The section 8(d) model rule requires manufacturers, importers, and processors of listed chemical substances and mixtures to submit to EPA copies and lists of unpublished health and safety studies. **Methyl ethyl ketone** is included on this list.
[40 CFR 716.120 (7/1/96)]**PEER REVIEWED**

CERCLA Reportable Quantities:

Persons in charge of vessels or facilities are required to notify the National Response Center (NRC) immediately, when there is a release of this designated hazardous substance, in an amount equal to or greater than its reportable quantity of 5000 lb or 2270 kg. The toll free number of the NRC is (800) 424-8802; In the Washington D.C. metropolitan area (202) 426-2675. The rule for determining when notification is required is stated in 40 CFR 302.4 (section IV. D.3.b).
[40 CFR 302.4 (7/1/96)]**PEER REVIEWED**

RCRA Requirements:

U159; As stipulated in 40 CFR 261.33, when 2-**butanone**, as a commercial chemical product or manufacturing chemical intermediate or an off-specification commercial chemical product or a manufacturing chemical intermediate, becomes a waste, it must be managed according to Federal and/or State hazardous waste regulations. Also defined as a hazardous waste is any residue, contaminated soil, water, or other debris resulting from the cleanup of a spill, into water or on dry land, of this waste. Generators of small quantities of this waste may qualify for partial exclusion from hazardous waste regulations (40 CFR 261.5).
[40 CFR 261.33 (7/1/96)]**PEER REVIEWED**

F005; When **methyl ethyl ketone** is a spent solvent, it is classified as a hazardous waste from a nonspecific source (F005), as stated in 40 CFR 261.31, and must be managed according to State and/or Federal hazardous waste regulations.
[40 CFR 261.31 (7/1/96)]**PEER REVIEWED**

Atmospheric Standards:

This action promulgates standards of performance for equipment leaks of Volatile Organic Compounds (VOC) in the Synthetic Organic Chemical Manufacturing Industry (SOCMI). The intended effect of these standards is to require all newly constructed, modified, and reconstructed SOCMI process units to use the best demonstrated system of continuous emission reduction for equipment leaks of VOC, considering costs, non air quality health and environmental impact and energy requirements. **Methyl ethyl ketone** is produced, as an intermediate or final product, by process units covered under this subpart.
[40 CFR 60.489 (7/1/87)]**PEER REVIEWED**

Listed as a hazardous air pollutant (HAP) generally known or suspected to cause serious health problems. The Clean Air Act, as amended in 1990, directs EPA to set standards requiring major sources to sharply reduce routine emissions of toxic pollutants. EPA is required to establish and phase in specific performance based standards for all air emission sources that emit one or more of the listed pollutants. **Methyl ethyl ketone** is included on this list.
[Clean Air Act as amended in 1990, Sect. 112 (b) (1) Public Law 101-549 Nov. 15, 1990]**QC REVIEWED**

State Drinking Water Guidelines:

(AZ) ARIZONA 170 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

(FL) FLORIDA 4,200 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

(MA) MASSACHUSETTS 350 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

(ME) MAINE 170 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

(MN) MINNESOTA 4000 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

(NC) NORTH CAROLINA 170 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water

Standards and Guidelines (11/93)] **QC REVIEWED**

(NH) NEW HAMPSHIRE 170 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

(NJ) NEW JERSEY 270 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

(WI) WISCONSIN 460 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

FDA Requirements:

Methyl ethyl ketone is an indirect food additive for use only as a component of adhesives.
[21 CFR 175.105 (4/1/96)]**PEER REVIEWED**

Methyl ethyl ketone is an indirect food additive polymer for use as a basic component of single and repeated use food contact surfaces. Residue limit 0.1% by weight of finished packaging cellophane.
[21 CFR 177.1200 (4/1/96)]**PEER REVIEWED**

Methyl ethyl ketone is a food additive permitted for direct addition to food for human consumption as a synthetic flavoring substance and adjuvant in accordance with the following conditions: 1) the quantity added to food does not exceed the amount reasonably required to accomplish its intended physical, nutritive, or other technical effect in food, and 2) when intended for use in or on food it is of appropriate food grade and is prepared and handled as a food ingredient.
[21 CFR 172.515 (4/1/96)]**PEER REVIEWED**

Allowable Tolerances:

Methyl ethyl ketone is exempted from the requirement of a tolerance when used as a solvent, cosolvent in accordance with good agricultural practice as inert (or occasionally active) ingredients in pesticide formulations applied to growing crops only.
[40 CFR 180.1001(d) (7/1/96)]**PEER REVIEWED**

Chemical/Physical Properties:

Molecular Formula:

C4-H8-O
PEER REVIEWED

Molecular Weight:

72.11

[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 1037]**PEER REVIEWED**

Color/Form:

COLORLESS LIQUID
[Sax, N.I. Dangerous Properties of Industrial Materials. 6th ed. New York, NY: Van Nostrand Reinhold, 1984. 549]**PEER REVIEWED**

Odor:

ACETONE-LIKE ODOR
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 1037]**PEER REVIEWED**

Sweet, pleasant, pungent
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Moderately sharp, fragrant, mint- or acetone-like odor.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 94-116. Washington, D.C.: U.S. Government Printing Office, June 1994. 36]**PEER REVIEWED**

Taste:

Taste threshold: 3.00x10+1 ppm in milk (media and purity not specified)
[Fazzalari, F.A. (ed.). Compilation of Odor and Taste Threshold Values Data. ASTM Data Series DS 48A (Committee E-18). Philadelphia, PA: American Society for Testing and Materials, 1978. 24]**PEER REVIEWED**

Taste threshold: 5.00x10+1 ppm in milk (purity not specified)
[Fazzalari, F.A. (ed.). Compilation of Odor and Taste Threshold Values Data. ASTM Data Series DS 48A (Committee E-18). Philadelphia, PA: American Society for Testing and Materials, 1978. 24]**PEER REVIEWED**

Boiling Point:

79.6 DEG C
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 1037]**PEER REVIEWED**

Melting Point:

-86 DEG C
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals,

Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 1037]**PEER REVIEWED**

Critical Temperature & Pressure:

CRITICAL TEMP: 504.5 DEG F= 262.5 DEG C= 535.7 DEG K; CRITICAL PRESSURE: 603 PSIA= 41.0 ATM= 4.15 MN/SQ M
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Density/Specific Gravity:

0.805 AT 20 DEG C/4 DEG C
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 1037]**PEER REVIEWED**

Heat of Combustion:

-13,480 BTU/LB= -7491 CAL/G= -313.6X10+5 JOULES/KG
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Heat of Vaporization:

LATENT HEAT OF VAPORIZATION: 191 BTU/LB= 106 CAL/G= 4.44X10+5 JOULES/KG
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Octanol/Water Partition Coefficient:

Log Kow = 0.29
[Hansch, C., Leo, A., D. Hoekman. Exploring QSAR - Hydrophobic, Electronic, and Steric Constants. Washington, DC: American Chemical Society., 1995. 9]**PEER REVIEWED**

Solubilities:

353,000 mg/l in water @ 10 deg C
[Verschueren, K. Handbook of Environmental Data on Organic Chemicals. 3rd ed. New York, NY: Van Nostrand Reinhold Co., 1996. 1281]**PEER REVIEWED**

SOL IN ALCOHOL, ETHER, ACETONE, & BENZENE
[Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 76th ed. Boca Raton, FL: CRC Press Inc., 1995-1996.,p. 3-101]**PEER REVIEWED**

190,000 mg/l in water @ 90 deg C

[Verschueren, K. Handbook of Environmental Data on Organic Chemicals. 3rd ed. New York, NY: Van Nostrand Reinhold Co., 1996. 1281]**PEER REVIEWED**

Spectral Properties:

MAX ABSORPTION (ALCOHOL): 273.5 NM (LOG E= 1.24); SADTLER REF NUMBER: 297 (IR, PRISM); 101 (IR, GRATING)
[Weast, R.C. (ed.). Handbook of Chemistry and Physics. 60th ed. Boca Raton, Florida: CRC Press Inc., 1979.,p. C-228]**PEER REVIEWED**

INDEX OF REFRACTION: 1.3814 @ 15 DEG C/D
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 1037]**PEER REVIEWED**

IR: 4788 (Coblentz Society Spectral Collection)
[Weast, R.C. and M.J. Astle. CRC Handbook of Data on Organic Compounds. Volumes I and II. Boca Raton, FL: CRC Press Inc. 1985.,p. V1 334]**PEER REVIEWED**

UV: 3-21 (Organic Electronic Spectral Data, Phillips et al, John Wiley & Sons, New York)
[Weast, R.C. and M.J. Astle. CRC Handbook of Data on Organic Compounds. Volumes I and II. Boca Raton, FL: CRC Press Inc. 1985.,p. V1 334]**PEER REVIEWED**

NMR: 76 (Varian Associates NMR Spectra Catalogue)
[Weast, R.C. and M.J. Astle. CRC Handbook of Data on Organic Compounds. Volumes I and II. Boca Raton, FL: CRC Press Inc. 1985.,p. V1 334]**PEER REVIEWED**

MASS: 68 (Atlas of Mass Spectral Data, John Wiley & Sons, New York)
[Weast, R.C. and M.J. Astle. CRC Handbook of Data on Organic Compounds. Volumes I and II. Boca Raton, FL: CRC Press Inc. 1985.,p. V1 334]**PEER REVIEWED**

Surface Tension:

24.6 dyne/cm @ 20 deg C
[Kirk-Othmer Encyclopedia of Chemical Technology. 4th ed. Volumes 1: New York, NY. John Wiley and Sons, 1991-Present.,p. V14 980]**PEER REVIEWED**

Vapor Density:

2.41 (Air= 1)
[Verschueren, K. Handbook of Environmental Data on Organic Chemicals. 3rd ed. New York, NY: Van Nostrand Reinhold Co., 1996. 1281]**PEER REVIEWED**

Vapor Pressure:

91 mm Hg at 25 deg C
[Alarie Y et al; Toxicol Appl Pharmacol 134: 92-99 (1995)]**PEER REVIEWED**

Relative Evaporation Rate:

EVAPORATION RATE: 2.7 (ETHER= 1)
[Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965. 421]**PEER REVIEWED**

Viscosity:

0.41 mPa.s @ 20 deg C
[Kirk-Othmer Encyclopedia of Chemical Technology. 4th ed. Volumes 1: New York, NY. John Wiley and Sons, 1991-Present.,p. V14 980]**PEER REVIEWED**

Other Chemical/Physical Properties:

CONSTANT BOILING MIXTURE WITH WATER, BP 73.4 DEG C, CONTAINS 88.7% **METHYL ETHYL KETONE (**MEK); SOLUBILITY OF WATER IN MEK IS 12.5% @ 25 DEG C
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 1037]**PEER REVIEWED**

SATURATED AIR CONCN IS 102,000 PPM @ 77.5 TORR, 20 DEG C
[American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices. 5th ed. Cincinnati, OH:American Conference of Governmental Industrial Hygienists, 1986. 395]**PEER REVIEWED**

HEAT OF SOLN (EST): -9 BTU/LB= -5 CAL/G= -0.2X10+5 JOULES/KG; RATIO OF SPECIFIC HEATS OF VAPOR (GAS): 1.075; REID VAPOR PRESSURE: 3.5 PSIA
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

CONVERSION FACTORS: 1 PPM= 2.94 MG/CU M; 1 MG/CU M= 0.340 PPM
[Verschueren, K. Handbook of Environmental Data on Organic Chemicals. 3rd ed. New York, NY: Van Nostrand Reinhold Co., 1996. 1282]**PEER REVIEWED**

Heat of fusion: 8.44 kJ/mole
[Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 76th ed. Boca Raton, FL: CRC Press Inc., 1995-1996.,p. 6-133]**PEER REVIEWED**

Coefficient of expansion= 0.00076/deg F; electrical conductivity= 1.0X10-7 ohms @ 25 deg C
[Flick, E.W. Industrial Solvents Handbook. 3rd ed. Park Ridge, NJ:

Noyes Publications, 1985. 473]**PEER REVIEWED**

Partition coefficients at 37 deg C for **methyl ethyl ketone** into blood= 202; into oil= 263.
[Sato A, Nakajima T; Scand J Work Environ Health 13: 81-93 (1987)]**PEER REVIEWED**

It is lighter than water ... and may be expected to float while rapidly dissolving.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, D.C.: Assoc. of American Railroads,Hazardous Materials Systems (BOE), 1987. 452]**PEER REVIEWED**

Henry's Law constant = 4.7X10-5 atm-cu m/mol at 25 deg C
[Bhattacharaya SK et al; Water Res 30: 3099-3105 (1996)]**PEER REVIEWED**

Chemical Safety & Handling:

DOT Emergency Guidelines:

Fire or explosion: HIGHLY FLAMMABLE: Will be easily ignited by heat, sparks or flames. Vapors may form explosive mixtures with air. Vapors may travel to source of ignition and flash back. Most vapors are heavier than air. They will spread along ground and collect in low or confined areas (sewers, basements, tanks). Vapor explosion hazard indoors, outdoors or in sewers. Some may polymerize (P) explosively when heated or involved in a fire. Runoff to sewer may create fire or explosion hazard. Containers may explode when heated. Many liquids are lighter than water.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-127]**PEER REVIEWED**

Health: Inhalation or contact with material may irritate or burn skin and eyes. Fire may produce irritating, corrosive and/or toxic gases. Vapors may cause dizziness or suffocation. Runoff from fire control may cause pollution.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-127]**PEER REVIEWED**

Public safety: CALL Emergency Response Telephone Number. ... Isolate spill or leak area immediately for at least 25 to 50 meters (80 to 160 feet) in all directions. Keep unauthorized personnel away. Stay upwind. Keep out of low areas. Ventilate closed spaces before entering.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the

Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-127]**PEER REVIEWED**

Protective clothing: Wear positive pressure self-contained breathing apparatus (SCBA). Structural firefighters' protective clothing will only provide limited protection.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-127]**PEER REVIEWED**

Evacuation: Large spill: Consider initial downwind evacuation for at least 300 meters (1000 feet). Fire: If tank, rail car or tank truck is involved in a fire, ISOLATE for 800 meters (1/2 mile) in all directions; also, consider initial evacuation for 800 meters (1/2 mile) in all directions.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-127]**PEER REVIEWED**

Fire: CAUTION: All these products have a very low flash point: Use of water spray when fighting fire may be inefficient. Small fires: Dry chemical, CO2, water spray or alcohol-resistant foam. Large fires: Water spray, fog or alcohol-resistant foam. Do not use straight streams. Move containers from fire area if you can do it without risk. Fire involving tanks or car/trailer loads: Fight fire from maximum distance or use unmanned hose holders or monitor nozzles. Cool containers with flooding quantities of water until well after fire is out. Withdraw immediately in case of rising sound from venting safety devices or discoloration of tank. ALWAYS stay away from the ends of tanks. For massive fire, use unmanned hose holders or monitor nozzles; if this is impossible, withdraw from area and let fire burn.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-127]**PEER REVIEWED**

Spill or leak: ELIMINATE all ignition sources (no smoking, flares, sparks or flames in immediate area). All equipment used when handling the product must be grounded. Do not touch or walk through spilled material. Stop leak if you can do it without risk. Prevent entry into waterways, sewers, basements or confined areas. A vapor suppressing foam may be used to reduce vapors. Absorb or cover with dry earth, sand or other non-combustible material and transfer to containers. Use clean non-sparking tools to collect absorbed material. Large spills: Dike far ahead of liquid spill for later disposal. Water spray may reduce vapor; but may not prevent ignition in closed spaces.
[U.S. Department of Transportation. 1996 North American Emergency

Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-127]**PEER REVIEWED**

First aid: Move victim to fresh air. Call emergency medical care. Apply artificial respiration if victim is not breathing. Administer oxygen if breathing is difficult. Remove and isolate contaminated clothing and shoes. In case of contact with substance, immediately flush skin or eyes with running water for at least 20 minutes. Wash skin with soap and water. Keep victim warm and quiet. Ensure that medical personnel are aware of the material(s) involved, and take precautions to protect themselves.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-127]**PEER REVIEWED**

Odor Threshold:

Odor low= 0.7375 mg/cu m; Odor high= 147.5 mg/cu m.
[Ruth JH; Am Ind Hyg Assoc J 47: A-142-51 (1986)]**PEER REVIEWED**

Detection limit in water: 5.00x10+1 ppm (purity not specified)
[Fazzalari, F.A. (ed.). Compilation of Odor and Taste Threshold Values Data. ASTM Data Series DS 48A (Committee E-18). Philadelphia, PA: American Society for Testing and Materials, 1978. 24]**PEER REVIEWED**

Recognition in air: 1.00x10+1 ppm (chemically pure)
[Fazzalari, F.A. (ed.). Compilation of Odor and Taste Threshold Values Data. ASTM Data Series DS 48A (Committee E-18). Philadelphia, PA: American Society for Testing and Materials, 1978. 24]**PEER REVIEWED**

Detection limit in air: 2.00x10+1 ppm (purity not specified)
[Fazzalari, F.A. (ed.). Compilation of Odor and Taste Threshold Values Data. ASTM Data Series DS 48A (Committee E-18). Philadelphia, PA: American Society for Testing and Materials, 1978. 24]**PEER REVIEWED**

Recognition in air: 5.50x10+1 ppm (purity not specified)
[Fazzalari, F.A. (ed.). Compilation of Odor and Taste Threshold Values Data. ASTM Data Series DS 48A (Committee E-18). Philadelphia, PA: American Society for Testing and Materials, 1978. 24]**PEER REVIEWED**

Skin, Eye and Respiratory Irritations:

High atm concn ... are irritating to the eyes, nose, and throat ... .
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1748]**PEER REVIEWED**

Vapor is irritating to human mucous membranes and conjuntivae @ 200 ppm after 15 min ... .
[Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984.,p. II-185]**PEER REVIEWED**

Fire Potential:

Highly flammable liquid.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 2239]**PEER REVIEWED**

NFPA Hazard Classification:

Health: 1. 1= Materials that, on exposure, would cause irritation, but only minor residual injury, including those requiring the use of an approved air-purifying respirator. These materials are only slightly hazardous to health and breathing protection is needed.
[National Fire Protection Guide. Fire Protection Guide on Hazardous Materials. 10 th ed. Quincy, MA: National Fire Protection Association, 1991.,p. 325M-69]**PEER REVIEWED**

Flammability: 3. 3= Includes Class IB and IC flammable liquids and materials that can be easily ignited under almost all normal temp conditions. Water may be ineffective in controlling or extinguishing fires in such materials.
[National Fire Protection Guide. Fire Protection Guide on Hazardous Materials. 10 th ed. Quincy, MA: National Fire Protection Association, 1991.,p. 325M-69]**PEER REVIEWED**

Reactivity: 0. 0= Includes materials that are normally stable, even under fire exposure conditions, and that do not react with water. Normal fire fighting procedures may be used.
[National Fire Protection Guide. Fire Protection Guide on Hazardous Materials. 10 th ed. Quincy, MA: National Fire Protection Association, 1991.,p. 325M-69]**PEER REVIEWED**

Flammable Limits:

LOWER 1.4% @ 93 DEG C (200 DEG F), UPPER 11.4% @ 93 DEG C (200 DEG F)
[National Fire Protection Guide. Fire Protection Guide on Hazardous Materials. 10 th ed. Quincy, MA: National Fire Protection Association, 1991.,p. 325M-69]**PEER REVIEWED**

Flash Point:

-9 deg C (16 deg F) closed cup
[National Fire Protection Guide. Fire Protection Guide on Hazardous Materials. 10 th ed. Quincy, MA: National Fire Protection Association, 1991.,p. 325M-69]**PEER REVIEWED**

22 deg F (Tag open cup)

[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 2239]**PEER REVIEWED**

Autoignition Temperature:

404 deg C (759 deg F)
[National Fire Protection Guide. Fire Protection Guide on Hazardous Materials. 10 th ed. Quincy, MA: National Fire Protection Association, 1991.,p. 325M-69]**PEER REVIEWED**

Fire Fighting Procedures:

ALC FOAM, DRY CHEMICAL, OR CARBON DIOXIDE
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

If material on fire or involved in fire: Do not extinguish fire unless flow can be stopped or safely confined. Use water in flooding quantities as fog. Solid streams of water may be ineffective. Cool all affected containers with flooding quantities of water. Apply water from as far a distance as possible. Use alcohol foam, dry chemical or carbon dioxide.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 704]**PEER REVIEWED**

Flammable. Flashback along vapor trail may occur. Vapor may explode if ignited in an enclosed area. Extinguish with dry chemical, alcohol foam, or carbon dioxide. Water may be ineffective on fire. Cool exposed containers with water.
[Prager, J.C. Environmental Contaminant Reference Databook Volume 1. New York, NY: Van Nostrand Reinhold, 1995. 350]**PEER REVIEWED**

Firefighting Hazards:

Flashback along vapor trail may occur.
[Prager, J.C. Environmental Contaminant Reference Databook Volume 1. New York, NY: Van Nostrand Reinhold, 1995. 350]**PEER REVIEWED**

Explosive Limits & Potential:

UPPER 10%; LOWER 1.8%
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 1171]**PEER REVIEWED**

Hazardous Reactivities & Incompatibilities:

Avoid copper
[DLA/DOD; Hazardous Materials Info System #6810-00-N00-0021 (1982)]**PEER REVIEWED**

Incompatible with chloroform, hydrogen peroxide, nitric acid, potassium t-butoxide, and 2-propanol.
[Bretherick, L. Handbook of Reactive Chemical Hazards. 4th ed. Boston, MA: Butterworth-Heinemann Ltd., 1990 465]**PEER REVIEWED**

MIXING **METHYL ETHYL KETONE** & CHLOROSULFONIC ACID OR OLEUM IN A CLOSED CONTAINER CAUSED THE TEMP & PRESSURE TO INCR.
[McEvoy G.K. (ed.). American Hospital Formulary Service-Drug Information 96. Bethesda, MD: American Society of Health-System Pharmacists, Inc. 1996 (Plus Supplements).,p. 491M-90]**PEER REVIEWED**

Strong oxidizers, amines, ammonia, inorganic acids, caustics, copper, isocyanates, pyridines.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 36]**QC REVIEWED**

Reaction with hydrogen peroxide + nitric acid forms a heat- and shock-sensitive explosive product. Ignition on contact with potassium t-butoxide. Mixture with 2-propanol will produce explosive peroxides during storage. Vigorous reaction with chloroform + alkali. Incompatible with chlorosulfonic acid; oleum.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 2239]**PEER REVIEWED**

Hazardous Decomposition:

MEK in air is rapidly decomposed by photochemical processes, mainly through oxidation by hydroxyl free radicals as well as some decomposition by direct photolysis ... /with a/ half-life of 5.4 hr for photochemical decomposition in urban atmospheres.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.36 (1993)]**PEER REVIEWED**

When heated to decomposition it emits acrid smoke and fumes.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 2239]**PEER REVIEWED**

Immediately Dangerous to Life or Health:

3000 ppm
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 36]**QC REVIEWED**

Protective Equipment & Clothing:

ORG CANISTER OR AIR PACK; PLASTIC GLOVES
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing

Office, 1984-5.]**PEER REVIEWED**

Skin contact should be avoided by the use of protective gloves; goggles may also be necessary to prevent eye contact. /Ketones/
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 1173]**PEER REVIEWED**

Breakthrough times greater than one hour reported by (normally) two or more testers were found for butyl rubber gloves.
[ACGIH; Guidelines Select of Chem Protect Clothing Volume #1 Field Guide p.68 (1983)]**PEER REVIEWED**

Breakthrough times less (usually significantly less) than one hour reported by (normally) two or more testers were found for natural rubber latex gloves, unsupported; neoprene/natural rubber blend; nitrile rubber glove, unsupported; polyethylene glove; polyvinyl alcohol glove, supported; polyvinyl chloride glove, unsupported; and viton, raw material.
[ACGIH; Guidelines Select of Chem Protect Clothing Volume #1 Field Guide p.68 (1983)]**PEER REVIEWED**

Wear appropriate personal protective clothing to prevent skin contact.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 36]**QC REVIEWED**

Wear appropriate eye protection to prevent eye contact.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 36]**QC REVIEWED**

Eyewash fountains should be provided in areas where there is any possbility that workers could be exposed to the substance; this is irrespective of the recommendation involving the wearing of eye protection.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 36]**QC REVIEWED**

Recommendations for respirator selection. Max concn for use: 3000 ppm. Respirator Class(es): Any supplied-air respirator operated in a continuous flow mode. eye protection needed. Any powered, air-purifying respirator with organic vapor cartridge(s). Eye protection needed. Any chemical cartridge respirator with a full facepiece and organic vapor cartridge(s). Any air-purifying, full-facepiece respirator (gas mask) with a chin-style, front- or back-mounted organic vapor canister. Any self-contained breathing apparatus with a full facepiece. Any supplied-air respirator with a full facepiece.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 36]**QC REVIEWED**

Recommendations for respirator selection. Condition: Emergency or planned entry into unknown concn or IDLH conditions: Respirator Class(es): Any self-contained breathing apparatus that has a full

facepiece and is operated in a pressure-demand or other positive pressure mode. Any supplied-air respirator that has a full face piece and is operated in pressure-demand or other positive pressure mode in combination with an auxiliary self-contained breathing apparatus operated in pressure-demand or other positive pressure mode.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 36]**QC REVIEWED**

Recommendations for respirator selection. Condition: Escape from suddenly occurring respiratory hazards: Respirator Class(es): Any air-purifying, full-facepiece respirator (gas mask) with a chin-style, front- or back-mounted organic vapor canister. Any appropriate escape-type, self-contained breathing apparatus.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 36]**QC REVIEWED**

Preventive Measures:

Work practices and industrial hygiene techniques should minimize the volatilization of ketones in the workroom air in order to ensure that the exposure limits are not exceeded. /Ketones/
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 1173]**PEER REVIEWED**

If material not on fire and not involved in fire: Keep sparks, flames, and other sources of ignition away. Keep material out of water sources and sewers. Build dikes to contain flow as necessary. Attempt to stop leak if without hazard. Use water spray to disperse vapors and dilute standing pools of liquid.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 704]**PEER REVIEWED**

Evacuation: If material leaking (not on fire) consider evacuation from downwind area based on amount of material spilled, location and weather conditions.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 704]**PEER REVIEWED**

Personnel protection: Avoid breathing vapors. Keep upwind. ... Do not handle broken packages without protective equipment. Wash away any material which may have contacted the body with copious amounts of water or soap and water.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 704]**PEER REVIEWED**

A major concern in the painting studio is solvents, /including **methyl ethyl ketone/. ...** Precautions include ... use of dilution and local exhaust ventilation, control of storage areas, disposal of solvent soaked rags in covered containers, minimizing skin exposure and the use of respirators and other personal protective equipment. The control of fire hazards is also important, since many of the solvents

are highly flammable.
[Hart C; J Environ Health 49 (5): 282-6 (1987)]**PEER REVIEWED**

SRP: Local exhaust ventilation should be applied wherever there is an incidence of point source emissions or dispersion of regulated contaminants in the work area. Ventilation control of the contaminant as close to its point of generation is both the most economical and safest method to minimize personnel exposure to airborne contaminants.
PEER REVIEWED

Contact lenses should not be worn when working with this chemical.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 36]**QC REVIEWED**

SRP: The scientific literature for the use of contact lenses in industry is conflicting. The benefit or detrimental effects of wearing contact lenses depend not only upon the substance, but also on factors including the form of the substance, characteristics and duration of the exposure, the uses of other eye protection equipment, and the hygiene of the lenses. However, there may be individual substances whose irritating or corrosive properties are such that the wearing of contact lenses would be harmful to the eye. In those specific cases, contact lenses should not be worn. In any event, the usual eye protection equipment should be worn even when contact lenses are in place.
PEER REVIEWED

SRP: Contaminated protective clothing should be segregated in such a manner so that there is no direct personal contact by personnel who handle, dispose, or clean the clothing. Quality assurance to ascertain the completeness of the cleaning procedures should be implemented before the decontaminated protective clothing is returned for reuse by the workers.
PEER REVIEWED

The worker should immediately wash the skin when it becomes contaminated.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 36]**QC REVIEWED**

Work clothing that becomes wet should be immediately removed due to its flammability hazard.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 36]**QC REVIEWED**

Stability/Shelf Life:

Stability during transport: stable
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Shipment Methods and Regulations:

No person may /transport,/ offer or accept a hazardous material for transportation in commerce unless

that person is registered in conformance ... and the hazardous material is properly classed, described, packaged, marked, labeled, and in condition for shipment as required or authorized by ... /the hazardous materials regulations (49 CFR 171-177)./
[49 CFR 171.2 (7/1/96)]**PEER REVIEWED**

The International Air Transport Association (IATA) Dangerous Goods Regulations are published by the IATA Dangerous Goods Board pursuant to IATA Resolutions 618 and 619 and constitute a manual of industry carrier regulations to be followed by all IATA Member airlines when transporting hazardous materials.
[IATA. Dangerous Goods Regulations. 38th ed. Montreal, Canada and Geneva, Switzerland: International Air Transport Association, Dangerous Goods Board, January, 1997. 179]**PEER REVIEWED**

The International Maritime Dangerous Goods Code lays down basic principles for transporting hazardous chemicals. Detailed recommendations for individual substances and a number of recommendations for good practice are included in the classes dealing with such substances. A general index of technical names has also been compiled. This index should always be consulted when attempting to locate the appropriate procedures to be used when shipping any substance or article.
[IMDG; International Maritime Dangerous Goods Code; International Maritime Organization p.3080 (1988)]**PEER REVIEWED**

Cleanup Methods:

The Hazardous Materials Technical Center (HMTC), an EPA emergency response cleanup services contractor cleaned up a **methyl ethyl ketone (**MEK) spill and decontaminated the groundwater. The spill cleanup involved removing low concentrations of MEK from groundwater. The spill was caused by an overturned tank truck containing 7200 gallons of MEK. MEK was directed into four dry wells that served as primary storm drainage. Immediately after the incident, 6000 gallons of water were pumped from the dry well; 2400 gallons of MEK were recovered from the water. About 1500 gallons of MEK were removed from the truck, and the remaining 3300 gallons of MEK either vaporized or entered an unsaturated zone. MEK concentrations up to 2200 mg/l were reduced to 50 ug/l before reinjection. Levels of MEK in the sample wells, production wells, and reinjection wells were reduced to nondetectable levels.
[Halvorsen F, Ohneck R; Proceedings of the National Conference on Hazardous Wastes and Environmental Emergencies p.193-95 (1985)]**PEER REVIEWED**

Environmental considerations -- air spill: Apply water spray or mist to knock down vapors.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 704]**PEER REVIEWED**

Environmental considerations -- water spill: Use natural barriers or oil spill control booms to limit spill travel. Remove trapped material with suction hoses.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 704]**PEER REVIEWED**

Environmental considerations -- land spill: Dig a pit, pond, lagoon, holding area to contain liquid or solid material. /SRP: If time permits, pits, ponds, lagoons, soak holes, or holding areas should be sealed with an impermeable flexible membrane liner./ Absorb bulk liquid with fly ash, cement powder, or commercial sorbents.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 704]**PEER REVIEWED**

Disposal Methods:

Generators of waste (equal to or greater than 100 kg/mo) containing this contaminant, EPA hazardous waste number F005, must conform with USEPA regulations in storage, transportation, treatment and disposal of waste.
[40 CFR 240-280, 300-306, 702-799 (7/1/96)]**PEER REVIEWED**

Generators of waste (equal to or greater than 100 kg/mo) containing this contaminant, EPA hazardous waste number U159, must conform with USEPA regulations in storage, transportation, treatment and disposal of waste.
[40 CFR 240-280, 300-306, 702-799 (7/1/96)]**PEER REVIEWED**

Incineration. Recommendable methods: Incineration, open burning, use as a fuel, evaporation, discharge to sewer. Peer-review: Potentially contains peroxides which may be explosive. Evaporate small amt only. (Peer-review conclusions of an IRPTC expert consultation (May 1985))
[United Nations. Treatment and Disposal Methods for Waste Chemicals (IRPTC File). Data Profile Series No. 5. Geneva, Switzerland: United Nations Environmental Programme, Dec. 1985. 116]**PEER REVIEWED**

A good candidate for fluidized bed incineration at a temperature range of 450 to 980 deg C and residence times of seconds for liquids and gases, and longer for solids. A good candidate for rotary kiln incineration at a temperature range of 820 to 1,600 deg C and residence times of seconds for liquids and gases, and hours for solids. A good candidate for liquid injection incineration at a temperature range of 650 to 1,600 deg C and a residence time of 0.1 to 2 seconds.
[USEPA; Engineering Handbook for Hazardous Waste Incineration p.3-14 (1981) EPA 68-03-3025]**PEER REVIEWED**

The following wastewater treatment technologies have been investigated for **methyl ethyl ketone:** solvent extraction and activated carbon.
[USEPA; Management of Hazardous Waste Leachate, EPA Contract No.68-03-2766 p.E-16 (1982)]**PEER REVIEWED**

Methyl ethyl ketone is a waste chemical stream constituent which may be subjected to ultimate disposal by controlled incineration.
[USEPA; Engineering Handbook for Hazardous Waste Incineration p.2-8 (1981) EPA 68-03-3025]**PEER REVIEWED**

Spray into incinerator or burn in paper packaging. More flammable solvent may be added.
[Prager, J.C. Environmental Contaminant Reference Databook Volume 1. New York, NY: Van Nostrand Reinhold, 1995. 349]**PEER REVIEWED**

Occupational Exposure Standards:

OSHA Standards:

Permissible Exposure Limit: Table Z-1 8-hr Time Weighted Avg: 200 ppm (590 mg/cu m).
[29 CFR 1910.1000 (7/1/98)]**QC REVIEWED**

Vacated 1989 OSHA PEL TWA 200 ppm (590 mg/cu m); STEL 300 ppm (885 mg/cu m) is still enforced in some states.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 360]**QC REVIEWED**

Threshold Limit Values:

8 hr Time Weighted Avg (TWA) 200 ppm; Short Term Exposure Limit (STEL) 300 ppm
[American Conference of Governmental Industrial Hygienists. Threshold Limit Values (TLVs) for Chemical Substances and Physical Agents Biological Exposure Indices for 1998. Cincinnati, OH: ACGIH, 1998. 49]**QC REVIEWED**

BEI (Biological Exposure Index): **Methyl ethyl ketone** in urine at end of shift is 2 mg/l. (1988 adoption)
[American Conference of Governmental Industrial Hygienists. Threshold Limit Values (TLVs) for Chemical Substances and Physical Agents Biological Exposure Indices for 1998. Cincinnati, OH: ACGIH, 1998. 102]**QC REVIEWED**

NIOSH Recommendations:

Recommended Exposure Limit: 10 Hr Time-Weighted Avg: 200 ppm (590 mg/cu m).
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 36]**QC REVIEWED**

Recommended Exposure Limit: 15 Min Short-Term Exposure Limit: 300 ppm (885 mg/cu m).
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 36]**QC REVIEWED**

Immediately Dangerous to Life or Health:

3000 ppm
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 36]**QC REVIEWED**

Manufacturing/Use Information:

Major Uses:

AS SOLVENT; IN THE SURFACE COATING INDUSTRY; MFR OF COLORLESS SYNTHETIC RESINS, SMOKELESS POWDER
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 1037]**PEER REVIEWED**

IN FABRIC COATING; IN ARTIFICIAL LEATHER MFR; IN LACQUER & VARNISH INDUSTRY; IN PHARMACEUTICALS & COSMETICS; IN SYNTHETIC RUBBER MFR; IN PRODUCTION OF LUBRICATING OILS
[Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965. 422]**PEER REVIEWED**

PAINT REMOVERS; CEMENTS & ADHESIVES; ORG SYNTHESIS; IN CLEANING FLUIDS
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 12th ed. New York, NY: Van Nostrand Rheinhold Co., 1993 768]**PEER REVIEWED**

SOLVENT FOR COATINGS-ESP VINYL, NITROCELLULOSE & ACRYLIC
[SRI]**PEER REVIEWED**

SOLVENT FOR ADHESIVES & MAGNETIC TAPES
[SRI]**PEER REVIEWED**

EXTRACTION SOLVENT FOR LUBE OIL DEWAXING, AZEOTROPIC SEPN
[SRI]**PEER REVIEWED**

SOLVENT FOR PRINTING INKS & IN CLEANING SOLNS
[SRI]**PEER REVIEWED**

EXTRACTION SOLVENT FOR HARDWOOD PULPING & VEGETABLE OIL
[SRI]**PEER REVIEWED**

OXIDN PROMOTER IN MFR OF TEREPHTHALIC ACID FROM P-XYLENE
[SRI]**PEER REVIEWED**

SOLVENT & COSOLVENT IN PESTICIDE FORMULATIONS
[SRI]**PEER REVIEWED**

FRAGRANCE & FLAVORING AGENT-EG, FOR CANDY & IN PERFUMES (FORMER USES)
[SRI]**PEER REVIEWED**

CATALYST IN THE PRODN OF HYDRAZINE (NON-USA USE)
[SRI]**PEER REVIEWED**

Used as a sterilizer for bacterial spores on surgical instruments, hypodermic needles/syringe, and dental instruments.
[Purdue University; National Pesticide Information Retrieval System (1988)]**PEER REVIEWED**

... Solvent ... required for the polymerization processing of polystyrene, acrylonitrile-butadiene-styrene,

and styrene-butadiene-rubber.
[Fishbein L; Industrial Hazards of Plastics and Synthetic Elastomers p.239-62 (1984)]**PEER REVIEWED**

Manufacturers:

Exxon Corp, Hq, 1251 Ave of the Americas, New York, NY 10020, (212) 333-1000; Exxon Chemical Co, division, Exxon Chemical Americas, PO Box 3272, Houston, TX 77001; Production site: Baton Rouge, LA 70821
[SRI. 1996 Directory of Chemical Producers-United States of America. Menlo Park, CA: SRI International, 1996. 744]**PEER REVIEWED**

Hoechst Celanese Corp, Hq, Route 202-206 N, Somerville, NJ 08876, (201) 231-2000; Hoechst Celanese Chemical Group, Inc, 1250 Mockingbird Lane, Dallas, TX 75356-9320; Production site: Pampa, TX 79065
[SRI. 1996 Directory of Chemical Producers-United States of America. Menlo Park, CA: SRI International, 1996. 744]**PEER REVIEWED**

Shell Oil Co, Hq, One Shell Plaza, PO Box 2463, Houston, TX 77252-2463, (713) 241-6161; Shell Chemical Co, division (address same as Hq); Production site: Norco, LA 70079
[SRI. 1996 Directory of Chemical Producers-United States of America. Menlo Park, CA: SRI International, 1996. 745]**PEER REVIEWED**

Methods of Manufacturing:

OBTAINED BY REFLUXING METHYL ACETOACETATE & DIL SULFURIC ACID, OR BY OXIDATION OF SECONDARY BUTYL ALCOHOL; ALSO BY FERMENTATION.
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 1037]**PEER REVIEWED**

DIRECT LIQUID-PHASE OXIDN OF BUTENES; BY-PRODUCT OF THE LIQUID DEHYDROGENATION OF BUTENES TO BUTADIENE
[SRI]**PEER REVIEWED**

Formulations/Preparations:

GRADES OF PURITY: 99.5+%
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

GRADE: TECHNICAL
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 12th ed. New York, NY: Van Nostrand Rheinhold Co., 1993 768]**PEER REVIEWED**

Consumption Patterns:

SOLVENT FOR VINYL COATINGS, 30%; SOLVENT FOR ADHESIVES, 18%; SOLVENT FOR

NITROCELLULOSE COATINGS, 13%; SOLVENT FOR ACRYLIC COATINGS, 11%; SOLVENT FOR OTHER COATINGS, 7%; SOLVENT FOR MAGNETIC TAPES, 7%; EXTRACTION SOLVENT FOR LUBE OIL DEWAXING, 5%; SOLVENT FOR PRINTING INKS, 5%; OTHER, 4% (1981)
[SRI]**PEER REVIEWED**

Projected growth figure through 1983 is 4%. Production of industrial coatings was 3.8% higher in 1978 than year before. Paint and varnish sales grew 13.6% during the same period.
[Kavaler. Chem Market Reporter 1980]**PEER REVIEWED**

CHEMICAL PROFILE: **Methyl Ethyl Ketone.** Coatings solvent, 50%; adhesives, 13%; magnetic tapes, 8%; lube oil dewaxing, 4%; printing inks, 3%; miscellaneous, 6%; exports, 16%.
[Kavaler AR; Chemical Marketing Reporter 232 (8): 50 (1987)]**PEER REVIEWED**

CHEMICAL PROFILE: **Methyl ethyl ketone.** Demand: 1986: 582 million lb; 1987: 600 million lb; 1991 /projected/: 600 million lb (Includes exports; in addition, 52 million lb were imported in 1986).
[Kavaler AR; Chemical Marketing Reporter 232 (8): 50 (1987)]**PEER REVIEWED**

Demand 1995: 582 million pounds; 1996: 545 million pounds; 2000: 550 million pounds (includes exports)
[Kavaler AR: Chemical Marketing Reporter. July 22, 1996]**PEER REVIEWED**

U. S. Production:

(1982) 4.68X10+8 lb
[USITC. Syn Org Chem-U.S. Prod/Sales (1982)]**PEER REVIEWED**

(1980) demand: 3.9X10+11 g
[Kavaler. Chem Market Reporter 1980]**PEER REVIEWED**

(1977) 2.32X10+11 G
[SRI]**PEER REVIEWED**

(1986) 2.44X10+11 g
[USITC SYN ORG CHEM-US PROD/SALES 1985 p.125]**PEER REVIEWED**

(1985) 5.37X10+8 lb
[USITC. SYN ORG CHEM-U.S. PROD/SALES 1985 p.266]**PEER REVIEWED**

(1987) 671,859X10+3 lb
[USITC. SYN ORG CHEM-U.S. PROD/SALES 1987 p.15-5]**PEER REVIEWED**

The demand for **methyl ethyl ketone** was 3.0X10+11 g in 1978, 3.7X10+11 g in 1979 and projected to be 3.6X10+11 g in 1983 (production plus imports)
[Kavaler. Chem Market Reporter 1980]**PEER REVIEWED**

U. S. Imports:

(1977) 3.58X10+10 G
[SRI]**PEER REVIEWED**

(1982) 1.90X10+10 G
[SRI]**PEER REVIEWED**

(1985) 3.51X10+10 g
[BUREAU OF THE CENSUS US IMPORTS FOR CONSUMPTION AND GENERAL IMPORTS 1985 p.-580]**PEER REVIEWED**

5.20X10+7 lb
[BUREAU OF THE CENSUS. US IMPORTS FOR CONSUMPTION AND GENERAL IMPORTS 1986 P. 1-526]**PEER REVIEWED**

1995 imports amounted to about 24 million pounds.
[Kavaler AR: Chemical Marketing Reporter. July 22, 1996]**PEER REVIEWED**

U. S. Exports:

(1978) 1.55X10+10 G
[SRI]**PEER REVIEWED**

(1983) 3.40X10+10 G
[SRI]**PEER REVIEWED**

(1985) 2.78X10+10 g
[BUREAU OF THE CENSUS U S EXPORTS, SCHEDULE E, 1986 p2-76]**PEER REVIEWED**

(1987) 4.63X10+6 lb
[BUREAU OF THE CENSUS. U S EXPORTS, SCHEDULE E, OCTOBER 1987, P.2-79]**PEER REVIEWED**

US exports totaled nearly 140 million pounds in 1995.
[Kavaler AR; Chemical MArketing Reporter. July 22, 1996]**PEER REVIEWED**

Laboratory Methods:

Clinical Laboratory Methods:

HEAD SPACE MASS SPECTROMETRIC SCREENING TECHNIQUE FOR VOLATILES IN BLOOD & POST-MORTEM TISSUES (LIVER, BRAIN, LUNG) IS DESCRIBED.
[URICH RW ET AL; J ANAL TOXICOL 1 (5): 195 (1977)]**PEER REVIEWED**

Venous blood sampled after 2 or more hr of exposure. Processed by Gas Chromatography, FID. Range: 0.1 to 8 ug/ml. Precision: 0.095 (1 ug/ml blood).
[U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational

Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. V1 8002-1]**PEER REVIEWED**

Methyl ethyl ketone in biofluid samples is analyzed using headspace chromatography with a flame ionization detector. The relative retention time is 0.816 min (relative to n-propanol 1.50 min).
[Sunshine, Irving (ed.) Methodology for Analytical Toxicology. Cleveland: CRC Press, Inc., 1975.,p. VII/7]**PEER REVIEWED**

A method is described for the determination of the concn of **methyl ethyl ketone** and its metabolites: 2-butanol, 3-hydroxy-2-**butanone**, and the meso- and d,l-isomers of 2,3-butanediol in urine. The analytes were isolated from urine by solid-phase extraction and analyzed by capillary gas chromatography. The recovery rates were 50-70% for the 2,3-butanediol isomers and 88-96% for the other analytes. The precision of the method ranged 5-12% (standard deviation %). The detection limit was 1.0 and 1.4 mg/l for meso- and d,l 2,3-butanediol, respectively, and ranged 0.1-0.15 mg/l for the other analytes.
[Kezic S, Monster AC; J Chromatogr 428 (2): 275-80 (1988)]**PEER REVIEWED**

Analytic Laboratory Methods:

METHOD IS BASED ON COLOR REACTION OF **METHYL ETHYL KETONE** WITH VANILLIN IN CONCN SULFURIC ACID.
[TYRAS H ET AL; CHEM ANAL (WARSAW) 21 (3): 647 (1976)]**PEER REVIEWED**

GLASS TUBE PACKED WITH ACTIVATED CHARCOAL IS USED TO TAKE AN INTEGRATED SAMPLE. GAS CHROMATOGRAPH EQUIPPED WITH A FLAME IONIZATION DETECTOR.
[WHITE LD ET AL; AM IND HYG ASSOC J 31 (2): 225 (1970)]**PEER REVIEWED**

ANALYTE: **METHYL ETHYL KETONE;** MATRIX: AIR; RANGE: 0.01 MG/SAMPLE; PROCEDURE: ADSORPTION ON CHARCOAL DESORPTION WITH CARBON DISULFIDE, GC; PRECISION: NOT GIVEN.
[U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. V1 2500-2]**PEER REVIEWED**

EPA Method 1624 - Volatile Organic Compounds By GC/MS: Grab samples in municipal and industrial discharges are collected. If residual chlorine is present, add sodium thiosulfate. Extraction is performed by a purge and trap apparatus. An isotope dilution gas chromatography/mass spectrometry method for the determination of volatile organic compounds in municipal and industrial discharges is described. Unlabeled **methyl ethyl ketone** has a minimum level of 50 ug/l and a mean retention time of 848 sec.
[40 CFR 136 (7/1/88)]**PEER REVIEWED**

EPA Method 8015: Nonhalogenated Volatile Organics. For the analysis of solid waste, a representative

sample (solid or liquid) is collected in a standard 40 ml glass screw-cap VOA vial equipped with a Teflon-faced silicone septum. Sample agitation, as well as contamination of the collected sample with air, must be avoided. Two VOA vials are filled per sample location, then placed in separate plastic bags for shipment and storage. Samples can be analyzed by direct injection or purge-and trap gas chromatography. A temperature program is used in the gas chromatograph to separate the organic compounds. Column 1 is an 8 ft by 0.1 in ID stainless steel or glass column packed with 1% SP-1000 on Carbopack-B 60/80 mesh or equivalent. Column 2 is a 6 ft by 0.1 in ID stainless steel or glass column packed with n-octane on Porasil-C 100/120 mesh (Durapak) or equivalent. Detection is achieved by a flame ionization detector (FID). Under the prescribed conditions, **methyl ethyl ketone** can be detected using this method. No statistical analysis was determined; specific method performance information will be provided as it becomes available.
[USEPA/Office of Solid Waste (OSW); Test Methods for Evaluating Solid Waste, Physical/Chemical Methods SW846 Methods (1986)]**PEER REVIEWED**

Sampling Procedures:

PORTABLE IR ANALYZERS MATED WITH MICROCOMPUTER ARE SUITABLE FOR ON-SITE MONITORING OF MIXTURES OF **METHYL ETHYL KETONE.**
[SYRJALA R; IND RES 19 (6): 81 (1977)]**PEER REVIEWED**

Calibrate each personal sampling pump with sampler in line. Break the ends and attach sampler to personal sampling pump with flexible tubing. Sample at flow rate between 0.01 and 0.2 l/min for total sample size of 1.0 to 12 l.
[U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. V1 2500-1]**PEER REVIEWED**

Activated charcoal, Ambersorb XE-348, and Amberlites XAD-2, XAD-4, and XAD-7 were evaluated as solid adsorbents for work-room air sampling of acetone, **methyl ethyl ketone,** methyl isobutyl ketone, methyl n-butyl ketone, cyclohexanone and isophorone. Activated charcoal had good capacity for the compounds investigated, but most ketones decomposed on this adsorbent during storage. Ambersorb XE-348 also showed good capacity for most of the ketones and decomposition was insignificant.
[Levin JO, Carleborg L; Ann Occup Hyg 31 (1): 31-8 (1987)]**PEER REVIEWED**

ANALYTE: 2-**BUTANONE**; MATRIX: AIR; RANGE: 380-1240 MG/CU M; PROCEDURE: ADSORPTION ON CHARCOAL, DESORPTION WITH CARBON DISULFIDE, GC.
[U.S. Department of Health, Education Welfare, Public Health Service. Center for Disease Control, National Institute for Occupational Safety Health. NIOSH Manual ofAnalytical Methods. 2nd ed. Volumes 1-7. Washington, DC: U.S. Government Printing Office, 1977-present.,p. V2 S3-1]**PEER REVIEWED**

Special References:

Special Reports:

PANSON RD; WINEK CL, CLIN TOXICOL 17 (2): 271 (1980). REVIEW ARTICLE ON HUMAN & ANIMAL TOXICITY & MGMNT.

OPDYKE DL J; FOOD COSMET TOXICOL 15 (6): 627 (1977). TOXICOLOGY, PREPARATION, PHYSICAL PROPERTIES, METABOLISM, PHARMACOLOGY, TERATOGENICITY, USE IN COSMETICS & IN FOODS ARE REVIEWED.

Yang RS H; Residue Rev 97: 121-43 (1986). The toxicology of **methyl ethyl ketone.** A review with many references on the manufacture, uses, and toxicity of **methyl ethyl ketone.**

Arbetarskyddsstyrelsen, Publikationsservice 171 (84): 133 (1985). Scientific basis for Swedish occupational standards.

USEPA; Health and Environmental Effects Profile for **Methyl Ethyl Ketone** p.80 (1988) EPA/600/X-85/363

DHHS/ATSDR; Toxicological Profile for 2-**Butanone** (1992) ATSDR/TP-91/08

WHO; Environmental Health Criteria 143: **Methyl Ethyl Ketone (**1993)

Synonyms and Identifiers:

Synonyms:

ACETONE, METHYL-
PEER REVIEWED

AETHYLMETHYLKETON (GERMAN)
PEER REVIEWED

BUTANONE
PEER REVIEWED

2-**BUTANONE**
PEER REVIEWED

3-**BUTANONE**
PEER REVIEWED

BUTANONE 2 (FRENCH)
PEER REVIEWED

Caswell No 569
PEER REVIEWED

EPA Pesticide Chemical Code 044103
PEER REVIEWED

Ethylmethylcetone (French)
PEER REVIEWED

ETHYLMETHYLKETON (DUTCH)
PEER REVIEWED

ETHYL METHYL KETONE
PEER REVIEWED

FEMA no 2170
PEER REVIEWED

KETONE, ETHYL METHYL
PEER REVIEWED

Meetco
PEER REVIEWED

MEK
PEER REVIEWED

METHYL ACETONE
PEER REVIEWED

Metiletilcetona (Spanish)
PEER REVIEWED

METILETILCHETONE (ITALIAN)
PEER REVIEWED

METYLOETYLOKETON (POLISH)
PEER REVIEWED

AI3-07540 (USDA)
PEER REVIEWED

Formulations/Preparations:

GRADES OF PURITY: 99.5+%
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

GRADE: TECHNICAL
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 12th ed. New York, NY: Van Nostrand Rheinhold Co., 1993 768]**PEER REVIEWED**

Shipping Name/ Number DOT/UN/NA/IMO:

UN 1193; Ethyl methyl ketone

IMO 3.2; Ethyl methyl ketone

Standard Transportation Number:

49 092 43; **Methyl ethyl ketone**

EPA Hazardous Waste Number:

U159; A toxic waste when a discarded commercial chemical product or manufacturing chemical intermediate or an off-specification commercial chemical product.

F005; A hazardous waste from nonspecific sources when a spent solvent.

RTECS Number:

NIOSH/EL6475000

Administrative Information:

Hazardous Substances Databank Number: 99

Last Revision Date: 20000324

Last Review Date: Reviewed by SRP on 9/18/1997

Update History:

Complete Update on 03/24/2000, 1 field added/edited/deleted.
Complete Update on 02/02/2000, 1 field added/edited/deleted.
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Complete Update on 09/21/1999, 1 field added/edited/deleted.
Complete Update on 08/26/1999, 1 field added/edited/deleted.
Complete Update on 07/20/1999, 5 fields added/edited/deleted.
Complete Update on 03/29/1999, 2 fields added/edited/deleted.
Field Update on 03/19/1999, 1 field added/edited/deleted.
Complete Update on 03/01/1999, 1 field added/edited/deleted.
Complete Update on 01/20/1999, 1 field added/edited/deleted.
Complete Update on 11/12/1998, 1 field added/edited/deleted.
Complete Update on 09/11/1998, 1 field added/edited/deleted.
Complete Update on 06/02/1998, 1 field added/edited/deleted.
Complete Update on 02/25/1998, 1 field added/edited/deleted.
Complete Update on 01/26/1998, 82 fields added/edited/deleted.
Field Update on 10/17/1997, 1 field added/edited/deleted.
Field Update on 09/08/1997, 5 fields added/edited/deleted.
Field Update on 08/13/1997, 5 fields added/edited/deleted.
Complete Update on 03/27/1997, 2 fields added/edited/deleted.
Complete Update on 02/24/1997, 1 field added/edited/deleted.
Complete Update on 12/11/1996, 1 field added/edited/deleted.
Complete Update on 06/06/1996, 1 field added/edited/deleted.
Complete Update on 04/09/1996, 8 fields added/edited/deleted.

Field Update on 01/18/1996, 1 field added/edited/deleted.
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Complete Update on 03/25/1994, 1 field added/edited/deleted.
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Complete Update on 08/04/1993, 1 field added/edited/deleted.
Field update on 12/10/1992, 1 field added/edited/deleted.
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Complete Update on 05/21/1990, 1 field added/edited/deleted.
Complete Update on 04/16/1990, 2 fields added/edited/deleted.
Complete Update on 01/11/1990, 2 fields added/edited/deleted.
Field update on 12/29/1989, 1 field added/edited/deleted.
Complete Update on 07/28/1989, 85 fields added/edited/deleted.
Field Update on 05/05/1989, 1 field added/edited/deleted.
Complete Update on 08/15/1988, 102 fields added/edited/deleted.
Complete Update on 03/31/1986

Record Length: 193690

METHYL ETHYL KETONE

CASRN: 78-93-3

For other data, click on the Table of Contents

Human Toxicity Excerpts:

HIGH ATM CONCN OF **METHYL ETHYL KETONE** IS IRRITATING TO THE EYES, NOSE, AND THROAT AND PROLONGED EXPOSURE MAY PRODUCE CNS DEPRESSION ... NO UNTOWARD EFFECTS HAVE BEEN REPORTED FOR CHRONIC EXPOSURE TO LOW CONCN. PROLONGED SKIN CONTACT MAY DEFAT THE SKIN AND PRODUCE DERMATITIS. IF SPLASHED IN THE EYES IT MAY PRODUCE PAINFUL IRRITATION AND CORNEAL INJURY.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1748]**PEER REVIEWED**

... WORKERS EXPOSED TO 300-500 PPM COMPLAINED OF HEADACHE, IRRITATION, AND NAUSEA. EXPOSURES TO 700 PPM LED TO NO PERMANENT UNTOWARD EFFECTS. MOMENTARY EXPOSURE TO 33,000 AND 100,000 PPM PRODUCED INTOLERABLE IRRITATION OF THE EYES, NOSE, AND THROAT.
[Clayton, G. D. and F. E. Clayton (eds.). Patty's Industrial Hygiene and Toxicology: Volume 2A, 2B, 2C: Toxicology. 3rd ed. New York: John Wiley Sons, 1981-1982. 4730]**PEER REVIEWED**

SHORT EXPOSURE OF WORKERS TO 500 PPM ... IN AIR PROVOKED NAUSEA AND VOMITING ... SEVERAL CASES OF PERIPHERAL NEUROPATHY ... OBSERVED /AFTER/ ACUTE PROLONGED OR REPEATED EXPOSURE. NEUROPATHY IS USUALLY SYMMETRICAL, PAINLESS WITH SENSORY LESIONS PREDOMINATING; IT MAY INVOLVE UPPER OR LOWER LIMBS; IN SOME CASES THE FINGERS HAVE BEEN AFFECTED FOLLOWING IMMERSION ... IN THE LIQUID. DERMATITIS ... REPORTED AFTER IMMERSION IN THE LIQUID AND AFTER EXPOSURE TO CONCN VAPORS. /KETONES/
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 1171]**PEER REVIEWED**

METHYL ETHYL KETONE IS IMPLICATED AS THE CAUSE OF RETROBULBAR NEURITIS IN PT WHO USED THE SOLVENT IN REMOVING PAINT FROM AN AIRPLANE HANGAR.
[BERG EF; ANN OPHTHALMOL 3 (12): 1351 (1971)]**PEER REVIEWED**

Exposure of the forearm for 1 hr/day for 6 consecutive days produced damage to the horny layer of the epithelium. ... **Methyl ethyl ketone** can defat and partially dehydrate the stratum corneum of human skin without producing irritation or inflammation.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1767]**PEER REVIEWED**

A workman splashed his eye accidentally /with **methyl ethyl ketone/,** but the next day had only slight conjunctival hyperemia and no residual corneal injury. Despite the mildness of the injury, in the next few days the affected eye developed severe anterior uveitis triggered by slight trauma.

[Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986. 617]**PEER REVIEWED**

Toxic effects of common organic solvents on workers /were/ examined. The most notable acute effects of occupational exposure to organic solvents are /CNS depression/ and other nerve dysfunctions. The common symptoms of short term exposure are fatigue, headache, nausea, sleep disturbance, and alteration in memory. Psychomotor performance of adverse effects on intellectual or memory functions are demonstrated with psychological test batteries after long-term occupational exposure to organic solvents. The mutagenic, carcinogenic, and toxicological effects of ... **methyl ethyl ketone ...** are summarized. ... In clinical observations, the effects of organic solvents can cause increased excretion of abnormal cells and protein in urine. This indicates the possible correlation between long-term exposure and renal disease.
[Bang KM; Health Hazards in the Occupational Environment 7 (3): 15-29 (1984)]**PEER REVIEWED**

A case of contact urticaria (CU) caused by **methyl ethyl ketone (**MEK) was reported. ... A cotton swab test with MEK to the normal skin on his forearm caused the skin to turn bright red. The spot was itchy, but no induration or edema was noticed. The reaction reached its maximum after 15 minutes and then gradually faded. The test was repeated after two days with the same results. Application of the same grade MEK to five medical staff members produced no reaction. ... MEK should be added to the list of agents that are not only irritants, but can also cause contact urticaria.
[Varigos GA, Nurse DS; Contact Dermatitis 15 (4): 259-60 (1986)]**PEER REVIEWED**

... Has a low toxicity following both acute and chronic exposures.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1748]**PEER REVIEWED**

HIGH ATM CONCN ... ARE IRRITATING TO THE EYES, NOSE, AND THROAT AND PROLONGED EXPOSURE MAY PRODUCE CNS DEPRESSION ... NO UNTOWARD EFFECTS HAVE BEEN REPORTED FOR CHRONIC EXPOSURE TO LOW CONCN. PROLONGED SKIN CONTACT MAY DEFAT THE SKIN AND PRODUCE DERMATITIS. IF SPLASHED IN THE EYES IT MAY PRODUCE PAINFUL IRRITATION AND CORNEAL INJURY.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1748]**PEER REVIEWED**

To determine whether unchanged solvent urinary concentration could be used as a biological exposure index, workers occupationally exposed to various solvents were studied. Nine unrelated groups (a total of 659 males) working in plastic boat, chemical, plastic button, paint, and shoe factories were studied. Urine samples were collected at the beginning of the workshift and at the end of the first half of the shift. A close relationship (correlation coefficient always above 0.85) between the average environmental solvent concentration (mg/cu m) measured in the breathing zone and the urinary concentration of unchanged solvent (ug/l) was observed.
[Ghittori S et al; Am Ind Hyg Assoc J 48 (9): 786-90 (1987)]**PEER REVIEWED**

... Seventy healthy male and female volunteers, 18 to 32 years old, with no previous prolonged exposure to solvents were exposed to 0 or 250 ppm acetone, 200 ppm MEK, or 125 ppm acetone plus 100 ppm MEK vapors for 4 hours in an exposure chamber. Expired air samples were collected before exposure, after 2 and 4 hours exposure, 90 minutes after exposure ended, and the next morning. Blood samples were collected on the day preceding exposure, at 2 or 4 hours of exposure, 2 hours after exposure ended, and the following day. Samples were analyzed for acetone and MEK by gas or gas/liquid chromatography. ... Blood MEK or acetone concentrations continued to increase throughout exposure, the increases between 2 and 4 hours being larger in the case of acetone. Acetone concentrations in the breath took longer to decrease than those of MEK. No interactive effects were noted in the combined exposures. Blood acetone and MEK concentrations were moderately correlated with their breath concentrations. Blood MEK and acetone concentrations tended to be lower in female subjects than in males; however, the differences were significant only for acetone in the combination exposure after 2 hours exposure and 90 minutes postexposure. ...
[Brown WD et al; The Changing Nature of Work and Workforce, Proceedings of the Third Joint US-Finish Science Symposium p.111-14 (1986)]**PEER REVIEWED**

A 47-yr old woman inadvertently ingested an unknown amt of MEK and was found unconscious, hyperventilating, and suffering from severe metabolic acidosis. Her plasma concn of MEK was 950 mg/L. She responded promptly to an infusion of sodium hydrogen carbonate and was discharged from the hospital after a wk. The metabolic effects of MEK ingestion by humans are not well characterized and it is uncertain that the acidosis was produced by MEK.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.81 (1993)]**PEER REVIEWED**

... exposure to 266-797 mg/cu m (90-270 ppm) for up to 4 hr/day caused his subjects to underestimate times of 5 to 30 sec ... on the other hand, found that a 4-hr exposure of human subjects to 590 mg/cu m (200 ppm) had no significant effect in a variety of behavioral test. These included psychomotor, visual vigilance, dual task, sensorimotor and psychological tests. Solvent mixtures of 295 mg MEK/cu m (100 ppm) and 298 mg acetone/cu m (125 ppm) similarly had no significant effect on the results of these behavioral tests.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.81 (1993)]**PEER REVIEWED**

MEK (0.1 mL) rubbed into volar forearm skin daily for 18 days and left uncovered did not produce persistent erythema or swelling ... A 5-min contact with 1.5 mL of analytical grade MEK confined to a 20-mm circle on the forearm produced a temporary whitening of the skin, but no visible erythema, alteration in cutaneous blood flow or other indication of irritation to the skin ... .
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.81 (1993)]**PEER REVIEWED**

Long-term exposure of 51 Italian workers to MEK produced indications of neurotoxicity with slightly, but not significantly, reduced nerve conduction velocities and various other symptoms such as headache, loss of appetite and weight, GI upset, dizziness, dermatitis and muscular hypotrophy, but no clinically recognizable neuropathy. ... There has been a brief report of chronic exposure of American workers, in a factory producing coated fabric, to 885-1770 mg MEK/cu m (300-600 ppm) in the apparent absence of other solvents. ... Workers complained of dermatoses and numbness of fingers and arms.

[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.82 (1993)]**PEER REVIEWED**

In a historical prospective morality study of 446 male workers in two MEK dewaxing plants, with an average follow up of 13.9 years, the observed deaths (46) were below the expected (55.51). There was a slight deficiency of deaths from neoplasms (13 observed; 14.26 expected) but there was a significant incr of deaths from tumors of the buccal cavity and pharynx (2 observed; 0.13 expected). However, there were significantly fewer deaths from lung cancer (1 observed; 6.02 expected). In view of the small numbers, it was concluded that there was no clear evidence of cancer hazard in these workers ... .
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.89 (1993)]**PEER REVIEWED**

The application of MEK to the forearm skin of two volunteers for 1 hr/day on six successive days damaged only the stratum corneum and that the dermal toxicity was similar to ethanol. Opdyke indicated that the application of 20 percent MEK in petrolatum to human forearm skin for 48 hr did not cause any irritation and that no sensitization reactions occurred when the same concentration was tested on 24 volunteers.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1767]**PEER REVIEWED**

Two cases of acute poisoning in a raincoat manufacturing operation where the seams were waterproofed with a resin dissolved in either acetone or MEK were reported. Samples of the workroom air indicated that the MEK concentration ranged from 398 to 561 ppm, whereas the acetone concentration ranged from 330 to 495 ppm. Two female employees were reportedly affected by the solvent vapors on different occasions. The first complained of stomach distress and watery eyes one morning, and later was found unconscious in a rest room. The employee had a strong acetone odor on her breath, but no acetonuria upon admission to the local hospital. She was treated with a CNS stimulant and awoke immediately, but complained of a severe headache. The patient was discharged from the hospital on the day following admission. The second case followed the first one by 1 day and was apparently less severe. The individual fainted and convulsed at the work site but regained consciousness immediately afterwards. At the hospital she was confused and had a headache, but after 1 hr of observation she was allowed to return home.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1767]**PEER REVIEWED**

A case study where a male patient attempted suicide by ingesting approximately 100 ml of an adhesive cement that contained 39 percent cyclohexanone, 28% MEK, 18% acetone was presented. The individual reportedly drank about 720 ml of sake (10 percent ethanol) 30 min prior to drinking the adhesive solution. The patient was unconscious when taken to a hospital about 2 hr after the ingestion of the solvent mixture. Gastric lavage, plasma exchange, and charcoal hemoperfusion were all performed, and the patient regained consciousness about 7 hr after ingestion; however, signs of systemic toxicity persisted. High blood concentrations of a cyclohexanone metabolite (cyclohexanal) were thought to be responsible for the coma, whereas the hyperglycemia was attributed to acetone.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New

York, NY: John Wiley & Sons Inc., 1993-1994. 1767]**PEER REVIEWED**

A case of retrobulbar neuritis in a sailor who was using large quantities of MEK as a paint remover was reported. The affected individual complained of blurred vision, light-headedness, and nausea after being exposed to MEK vapor for 1.5 hr. Upon admission to a military hospital, the patient's near- and far-field visual acuity was reduced and blind spots were markedly enlarged when a white target was viewed. An ophthalmoscopic examination, however, did not reveal any abnormalities. Clinical testing on the day of admission revealed elevations in blood methanol and formaldehyde. Visual acuity returned to normal within 2 days of admission; however, the blood methanol levels did not return to normal until the sixth day of hospitalization. /It was/ concluded that MEK was the causative agent for the optic nerve damage that was observed. The MEK was assumed to have been systemically absorbed both dermally and through the lungs and then partially metabolized to methanol, which subsequently affected the optic nerve and cerebral cortex.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1767]**PEER REVIEWED**

A case of toxic encephalopathy with dementia and cerebellar ataxia in a 38-year-old male who spray-painted a truck in an unventilated garage with a paint that contained toluene, MEK, and propylene glycol. As time passed following the exposure, the individual began to experience memory problems along with headaches, shortness of breath, appetite and sleep disturbances, ataxia, and suicidal depression. Neuropsychological evaluations over a 2.5 year period revealed distinct cognitive, motor, and behavioral changes.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1769]**PEER REVIEWED**

The pharmacokinetics of MEK in 70 male and female volunteers following a 4-hr inhalation exposure either alone (200 ppm) or in combination with acetone (225 ppm, 1:1.25 ratio) was described. Blood and expired air elimination data for the MEK-exposed individuals revealed on average that (1) MEK steady-state breath levels of about 10 to 12 ppm were attained, (2) non-steady-state peak blood levels of 3 to 4 ug/ml occurred, (3) no significant difference in uptake or elimination was observed for males and females, and (4) no appreciable interaction affecting elimination took place with the combined exposures.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1769]**PEER REVIEWED**

METHYL ETHYL KETONE

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For other data, click on the Table of Contents

Skin, Eye and Respiratory Irritations:

High atm concn ... are irritating to the eyes, nose, and throat ... .
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1748]**PEER REVIEWED**

Vapor is irritating to human mucous membranes and conjuntivae @ 200 ppm after 15 min ... .
[Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984.,p. II-185]**PEER REVIEWED**

METHYL ETHYL KETONE

CASRN: 78-93-3

For other data, click on the Table of Contents

Probable Routes of Human Exposure:

NIOSH has est worker exposure to **methyl ethyl ketone** at 3,031,000 ...
[Sittig, M. Handbook of Toxic and Hazardous Chemicals and Carcinogens, 1985. 2nd ed. Park Ridge, NJ: Noyes Data Corporation, 1985. 601]**PEER REVIEWED**

Artificial leather workers /are at risk of exposure/.
[Arena, J.M. and Drew, R.H. (eds.) Poisoning-Toxicology, Symptoms, Treatments. 5th ed. Springfield, IL: Charles C. Thomas Publisher, 1986. 358]**PEER REVIEWED**

NIOSH (NOES Survey 1981-1983) has statistically estimated that 1,221,857 workers (201,308 of these are female) are potentially exposed to **methyl ethyl ketone** in the US(1). Occupational exposure may be through inhalation and dermal contact with this compound at workplaces where **methyl ethyl ketone** is produced or used(SRC). The 8 hour TWA exposure to **methyl ethyl ketone** was 45.4 ppm in a survey of 50 occupationally exposed male subjects working in a magnetic videotape producing factory(2). These workers had average concns of **methyl ethyl ketone** of 2 ppm and 1.4 mg/l in breath and blood samples respectively(2). The mean concn of **methyl ethyl ketone** in the breathing zones of 47 US plants using polyurethane coatings was 4.33 ppm(3). **Methyl ethyl ketone** was detected in the breathing zones in 20 of 70 samples (mean concn 12 mg/cu m) obtained from autobody shops and spray paint shops in Australia(4).
[(1) NIOSH; National Occupational Exposure Survey (NOES) (1983) (2) Sia Gl et al; Environ Monit Assess 19: 401-11 (1991) (3) Myer HE et al; Am Ind Hyg Assoc J 54: 663-70 (1993) (4) Winder C, Turner PJ; Ann Occup Hyg 36: 385-94 (1992)]**PEER REVIEWED**

The general population may be exposed to **methyl ethyl ketone** through the use of commercially available products containing this compound such as paints, adhesives, and rubber cements(SRC). Exposure will also arise from inhalation of ambient air, ingestion of drinking water and food that contains **methyl ethyl ketone(**SRC). The average blood concn of **methyl ethyl ketone** in 600 non-occupationally exposed individuals in the US was 7.1 ppb(1).
[(1) Ashley DL et al; Clin Chem 40: 1401-04 (1994)]**PEER REVIEWED**

METHYL ETHYL KETONE

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For other data, click on the Table of Contents

Body Burden:

Detected in 5 of 8 samples of mother's milk from 4 USA urban areas.
[(1) Pellizzari ED et al; Bull Environ Contam Toxicol 28: 322-8 (1982)]**PEER REVIEWED**

The kinetics of inhaled **methyl ethyl ketone (**MEK) in human volunteers was studied in an exposure chamber. Relative pulmonary uptake was about 53% throughout a 4 hr exposure period at 200 ppm. Blood MEK concentration rose steadily until the end of exposure. Repeated bicycle exercise increased the overall blood MEK level markedly in comparison to sedentary activity, with transient peaks in association with cycling; thus blood MEK concentration depended both on the rate of uptake and the amount taken up. Only 3% of the absorbed dose was excreted unchanged by exhalation. A well known metabolite of MEK, 2,3-butanediol, was detected in the urine with maximum rates of excretion at about 6 to 12 hr from the beginning of exposure. About 2% of the MEK dose taken up by the lungs was excreted in the urine as 2,3-butanediol. ... Elimination of MEK in blood appeared to exhibit two phases: the initial alpha-phase (T1/2= 30 min; kel alpha= 0.023) over the first post-exposure hour, followed by the terminal beta-phase (T1/2= 81 min; kel beta= 0.009).
[Liira J et al; Int Arch Occup Environ Health 60 (3): 195-200 (1988)]**PEER REVIEWED**

Worker exposures were investigated in April 1983 at the Hoover Company, North Canton, Ohio. ... Area and personal air samples for numerous contaminants were collected and nonionizing radiation levels were measured. ... General medical questionnaires and blood tests for **methyl ethyl ketone (**MEK) were given to exposed workers. ... No respiratory symptoms or pulmonary function disorders were identified in the foundry workers, and MEK was detected in the blood of only one worker at 1.4 ug/ml. ...
[NIOSH; Health Hazard Evaluation Report No. HETA-82-280-1407 (1984)]**PEER REVIEWED**

METHYL ETHYL KETONE

CASRN: 78-93-3

For other data, click on the Table of Contents

Emergency Medical Treatment:

Emergency Medical Treatment:

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The following Overview, *** KETONES ***, is relevant for this HSDB record chemical.

Life Support:

- This overview assumes that basic life support measures have been instituted.

Clinical Effects:

SUMMARY OF EXPOSURE

0.2.1.1 ACUTE EXPOSURE

- ACUTE EXPOSURE (ORAL) - Most available information concerns inhalational or dermal exposure. A few cases involving ingestion of **methyl ethyl ketone (**and co-ingestants) or ketone peroxide (with co-ingestants) have resulted in CNS depression, respiratory depression or corrosive effects and sequelae.
- ACUTE INHALATION - The effects vary, depending on extent and duration of exposure. Eye, nose and throat irritation, nausea, headache, vertigo, incoordination, CNS depression, narcosis and cardiorespiratory failure can occur. In most cases, recovery is usually rapid and complete.
- CHRONIC EXPOSURE - The major concern with chronic exposure is axonal neuropathy with secondary myelin damage; usually manifested as paresthesias and muscle weakness. Only six-carbon, linear chain ketones metabolized to gamma-diketones (such as methyl n-butyl ketone) are implicated.
- EYE EXPOSURE - Splash contact causes irritation, which may be slight, moderate, or severe, depending on the ketone. Vapors can cause irritation and lacrimation.

- ROUTES OF EXPOSURE - Ketones are absorbed by ingestion, inhalation, and dermal exposure.
- RELATED COMPOUNDS - Exposure to ketone solvents (**methyl ethyl ketone,** methyl isobutyl ketone, etc) must be distinguished from exposure to the peroxides of these same ketones. KETONE PEROXIDES are highly reactive and corrosive. Management of ketone peroxide exposure is discussed in a separate document.

HEENT

0.2.4.1 ACUTE EXPOSURE

- Splash contact causes irritation, which may be slight, moderate, or severe, depending on the specific ketone; vapors may cause irritation and lacrimation.

CARDIOVASCULAR

0.2.5.1 ACUTE EXPOSURE

- Tachycardia may occur.

RESPIRATORY

0.2.6.1 ACUTE EXPOSURE

- Ingestion of significant amounts may cause respiratory depression. Inhalation exposure may produce an anesthetic type of respiratory depression, dyspnea, and gasping. Pulmonary aspiration may result in chemical pneumonitis.

NEUROLOGIC

0.2.7.1 ACUTE EXPOSURE

- Acute inhalation exposure causes a progression of CNS effects, from headache, vertigo, incoordination, narcosis, dizziness, and tremor, to coma. Peripheral neuropathy has been reported following exposure to methyl-n-butyl ketone and 2,5-hexanedione. Trimethylnonanone is not associated with narcosis.
- Chronic exposure causes axonal neuropathy with secondary myelin damage, usually manifested as paresthesias and muscle weakness. Only six-carbon, linear chain ketones metabolized to gamma-diketones (such as methyl n-butyl ketone) are implicated.

GASTROINTESTINAL

0.2.8.1 ACUTE EXPOSURE

- Nausea and vomiting may occur.

HEPATIC

0.2.9.1 ACUTE EXPOSURE

- Ketones may potentiate the hepatotoxicity of halogenated hydrocarbons. They may also inhibit aromatic hydrocarbon metabolism.

ACID-BASE

0.2.11.1 ACUTE EXPOSURE

- Metabolic acidosis has been reported.

DERMATOLOGIC

0.2.14.1 ACUTE EXPOSURE

- Skin exposure to the liquid or vapor may result in dermatitis and paresthesias of affected areas. Contact urticaria has also been reported.

REPRODUCTIVE HAZARDS

- Limited studies have generally documented little or no effect of ketones on reproduction in experimental animals. Human data is lacking. 2,5-Hexanedione has an effect on spermatogenesis in male experimental animals.

CARCINOGENICITY

0.2.21.1 IARC CATEGORY

- The ketones are generally unclassified by IARC. Those agents evaluated by IARC have been classified as having insufficient evidence to determine human carcinogenicity.

0.2.21.2 HUMAN OVERVIEW

- No adequate human studies exist for the agents in this category.

0.2.21.3 ANIMAL OVERVIEW

- Experimental animal studies are limited, but are generally negative, and agents in this group have little mutagenic activity.

GENOTOXICITY

- Extremely limited data is available for this class of agents. For many specific ketones, no data is available. Some studies report positive findings, but this category of agents appears to be generally non-mutagenic or only weakly mutagenic.

Laboratory:

- Plasma ketone levels are not clinically useful.
- If pulmonary aspiration is suspected, monitor chest x-ray and arterial blood gases or pulse oximetry.

Treatment Overview:

ORAL EXPOSURE

- With ingestion of small amounts the major concern is pulmonary aspiration and gastrointestinal decontamination is not recommended. With ingestion of large amounts there is potential for systemic toxicity from gastrointestinal absorption and GI decontamination is suggested, keeping in mind that pulmonary aspiration is still a concern.
- If the patient is obtunded, seizing, or has significant alterations in mental status, a cuffed endotracheal tube should be inserted prior to gastric aspiration.
  1. For moderate ingestions (less than 100 milliliters) activated charcoal alone is recommended.
  2. For large ingestions that have occurred within the past hour, careful gastric aspiration followed by activated charcoal is recommended.
     a. The lavage tube should be flexible, well lubricated with a water soluble gel to minimize gagging and vomiting, and of a large enough diameter to minimize vomiting of gastric contents around the tube and potential pulmonary aspiration.
     b. After the tube is in place, evacuate gastric contents rapidly. Repeated instillation of fluid to wash out the stomach is NOT suggested as it probably does not significantly enhance the removal of liquids and may enhance the potential for pulmonary aspiration.
     c. Instill activated charcoal prior to withdrawing the tube.
     d. For ingestions that have occurred more than 2 hours ago, gastric decontamination is not likely to be of benefit and is generally not warranted.
- Administer activated charcoal for moderate or large ingestions.
  1. ACTIVATED CHARCOAL: Administer charcoal as slurry (240 mL water/30 g charcoal). Usual dose: 25 to 100 g in adults/adolescents, 25 to 50 g in children (1 to 12 years), and 1 g/kg in infants less than 1 year old.
- ACIDOSIS - Correct severe acidosis (pH < 7.1) with intravenous sodium bicarbonate. About 1 to 2 milliequivalents/kilogram is a useful starting dose. Monitor arterial blood gases to guide bicarbonate therapy.

INHALATION EXPOSURE

- DECONTAMINATION: Move patient to fresh air. Monitor

for respiratory distress. If cough or difficulty in breathing develops, evaluate for respiratory tract irritation, bronchitis, or pneumonitis. Administer 100 percent humidified supplemental oxygen with assisted ventilation as required.

EYE EXPOSURE

- DECONTAMINATION: Exposed eyes should be irrigated with copious amounts of tepid water for at least 15 minutes. If irritation, pain, swelling, lacrimation, or photophobia persist, the patient should be seen in a health care facility.

DERMAL EXPOSURE

- DECONTAMINATION: Wash exposed area extremely thoroughly with soap and water. A physician may need to examine the area if irritation or pain persists.
- Treat dermal irritation or burns with standard topical therapy. Patients developing dermal hypersensitivity reactions may require treatment with systemic or topical corticosteroids or antihistamines.

Range of Toxicity:

- The minimal toxic or lethal dose is variable and not well defined. Toxic effects following inhalation exposure depend on air concentration, time of exposure and underlying diseases.
- Exposure to airborne concentrations greater than 300 ppm of **methyl ethyl ketone** may result in discomfort and CNS depression. Methyl-isobutyl ketone produces irritation at an airborne concentration of 100 ppm (Hjelm et al, 1990).

[Rumack BH: POISINDEX(R) Information System. Micromedex, Inc., Englewood, CO, 2001; CCIS Volume 107, edition exp February, 2001. Hall AH & Rumack BH (Eds):TOMES(R) Information System. Micromedex, Inc., Englewood, CO, 2001; CCIS Volume 107, edition exp February, 2001.]
PEER REVIEWED

Antidote and Emergency Treatment:

For immediate first aid: Ensure that adequate decontamination has been carried out. If victim is not breathing, start artificial respiration, preferably with a demand-valve resuscitator, bag-valve-mask device, or pocket mask as trained. Perform CPR if necessary. Immediately flush contaminated eyes with gently flowing water. Do not induce vomiting. If vomiting occurs, lean patient forward or place on left side (head-down position, if possible) to maintain an open airway and prevent aspiration. Keep victim quiet and maintain normal body temperature. Obtain medical attention. /Ketones and related compounds/
[Bronstein, A.C., P.L. Currance; Emergency Care for Hazardous

Materials Exposure. 2nd ed. St. Louis, MO. Mosby Lifeline. 1994. 237]**PEER REVIEWED**

For basic treatment: Establish a patent airway. Suction if necessary. Watch for signs of respiratory insufficiency and assist ventilations if necessary. Administer oxygen by nonrebreather mask at 10 to 15 L/min. Monitor for pulmonary edema and treat if necessary. ... For contamination, flush eyes immediately with water. Irrigate each eye continuously with normal saline during transport. ... Do not use emetics. For ingestion, rinse mouth and administer 5 mL/kg up to 200 mL of water for dilution if the patient can swallow, has a strong gag reflex, and does not drool. Administer activated charcoal ... . /Ketones and related compounds/

[Bronstein, A.C., P.L. Currance; Emergency Care for Hazardous Materials Exposure. 2nd ed. St. Louis, MO. Mosby Lifeline. 1994. 237]**PEER REVIEWED**

METHYL ETHYL KETONE

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Emergency Medical Treatment:

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The following Overview, *** KETONES ***, is relevant for this HSDB record chemical.

Life Support:

- This overview assumes that basic life support measures have been instituted.

Clinical Effects:

SUMMARY OF EXPOSURE

0.2.1.1 ACUTE EXPOSURE

- ACUTE EXPOSURE (ORAL) - Most available information concerns inhalational or dermal exposure. A few cases involving ingestion of **methyl ethyl ketone (**and co-ingestants) or ketone peroxide (with co-ingestants) have resulted in CNS depression, respiratory depression or corrosive effects and sequelae.
- ACUTE INHALATION - The effects vary, depending on extent and duration of exposure. Eye, nose and throat irritation, nausea, headache, vertigo, incoordination, CNS depression, narcosis and cardiorespiratory failure can occur. In most cases, recovery is usually rapid and complete.
- CHRONIC EXPOSURE - The major concern with chronic exposure is axonal neuropathy with secondary myelin damage; usually manifested as paresthesias and muscle weakness. Only six-carbon, linear chain ketones metabolized to gamma-diketones (such as methyl n-butyl ketone) are implicated.
- EYE EXPOSURE - Splash contact causes irritation, which may be slight, moderate, or severe, depending on the ketone. Vapors can cause irritation and lacrimation.
- ROUTES OF EXPOSURE - Ketones are absorbed by ingestion, inhalation, and dermal exposure.

- RELATED COMPOUNDS - Exposure to ketone solvents (**methyl ethyl ketone,** methyl isobutyl ketone, etc) must be distinguished from exposure to the peroxides of these same ketones. KETONE PEROXIDES are highly reactive and corrosive. Management of ketone peroxide exposure is discussed in a separate document.

HEENT

0.2.4.1 ACUTE EXPOSURE

- Splash contact causes irritation, which may be slight, moderate, or severe, depending on the specific ketone; vapors may cause irritation and lacrimation.

CARDIOVASCULAR

0.2.5.1 ACUTE EXPOSURE

- Tachycardia may occur.

RESPIRATORY

0.2.6.1 ACUTE EXPOSURE

- Ingestion of significant amounts may cause respiratory depression. Inhalation exposure may produce an anesthetic type of respiratory depression, dyspnea, and gasping. Pulmonary aspiration may result in chemical pneumonitis.

NEUROLOGIC

0.2.7.1 ACUTE EXPOSURE

- Acute inhalation exposure causes a progression of CNS effects, from headache, vertigo, incoordination, narcosis, dizziness, and tremor, to coma. Peripheral neuropathy has been reported following exposure to methyl-n-butyl ketone and 2,5-hexanedione. Trimethylnonanone is not associated with narcosis.
- Chronic exposure causes axonal neuropathy with secondary myelin damage, usually manifested as paresthesias and muscle weakness. Only six-carbon, linear chain ketones metabolized to gamma-diketones (such as methyl n-butyl ketone) are implicated.

GASTROINTESTINAL

0.2.8.1 ACUTE EXPOSURE

- Nausea and vomiting may occur.

HEPATIC

0.2.9.1 ACUTE EXPOSURE

- Ketones may potentiate the hepatotoxicity of halogenated hydrocarbons. They may also inhibit aromatic hydrocarbon metabolism.

ACID-BASE

0.2.11.1 ACUTE EXPOSURE

- Metabolic acidosis has been reported.

DERMATOLOGIC

0.2.14.1 ACUTE EXPOSURE

- Skin exposure to the liquid or vapor may result in dermatitis and paresthesias of affected areas. Contact urticaria has also been reported.

REPRODUCTIVE HAZARDS

- Limited studies have generally documented little or no effect of ketones on reproduction in experimental animals. Human data is lacking. 2,5-Hexanedione has an effect on spermatogenesis in male experimental animals.

CARCINOGENICITY

0.2.21.1 IARC CATEGORY

- The ketones are generally unclassified by IARC. Those agents evaluated by IARC have been classified as having insufficient evidence to determine human carcinogenicity.

0.2.21.2 HUMAN OVERVIEW

- No adequate human studies exist for the agents in this category.

0.2.21.3 ANIMAL OVERVIEW

- Experimental animal studies are limited, but are generally negative, and agents in this group have little mutagenic activity.

GENOTOXICITY

- Extremely limited data is available for this class of agents. For many specific ketones, no data is available. Some studies report positive findings, but this category of agents appears to be generally non-mutagenic or only weakly mutagenic.

Laboratory:

- Plasma ketone levels are not clinically useful.
- If pulmonary aspiration is suspected, monitor chest x-ray and arterial blood gases or pulse oximetry.

Treatment Overview:

ORAL EXPOSURE

- With ingestion of small amounts the major concern is pulmonary aspiration and gastrointestinal decontamination is not recommended. With ingestion of large amounts there is potential for systemic toxicity from gastrointestinal absorption and GI decontamination is suggested, keeping in mind that pulmonary aspiration is still a concern.
- If the patient is obtunded, seizing, or has significant alterations in mental status, a cuffed endotracheal tube should be inserted prior to gastric aspiration.
  1. For moderate ingestions (less than 100 milliliters) activated charcoal alone is recommended.
  2. For large ingestions that have occurred within the past hour, careful gastric aspiration followed by activated charcoal is recommended.
     a. The lavage tube should be flexible, well lubricated with a water soluble gel to minimize gagging and vomiting, and of a large enough diameter to minimize vomiting of gastric contents around the tube and potential pulmonary aspiration.
     b. After the tube is in place, evacuate gastric contents rapidly. Repeated instillation of fluid to wash out the stomach is NOT suggested as it probably does not significantly enhance the removal of liquids and may enhance the potential for pulmonary aspiration.
     c. Instill activated charcoal prior to withdrawing the tube.
     d. For ingestions that have occurred more than 2 hours ago, gastric decontamination is not likely to be of benefit and is generally not warranted.
- Administer activated charcoal for moderate or large ingestions.
  1. ACTIVATED CHARCOAL: Administer charcoal as slurry (240 mL water/30 g charcoal). Usual dose: 25 to 100 g in adults/adolescents, 25 to 50 g in children (1 to 12 years), and 1 g/kg in infants less than 1 year old.
- ACIDOSIS - Correct severe acidosis (pH < 7.1) with intravenous sodium bicarbonate. About 1 to 2 milliequivalents/kilogram is a useful starting dose. Monitor arterial blood gases to guide bicarbonate therapy.

INHALATION EXPOSURE

- DECONTAMINATION: Move patient to fresh air. Monitor

for respiratory distress. If cough or difficulty in breathing develops, evaluate for respiratory tract irritation, bronchitis, or pneumonitis. Administer 100 percent humidified supplemental oxygen with assisted ventilation as required.

EYE EXPOSURE

- DECONTAMINATION: Exposed eyes should be irrigated with copious amounts of tepid water for at least 15 minutes. If irritation, pain, swelling, lacrimation, or photophobia persist, the patient should be seen in a health care facility.

DERMAL EXPOSURE

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- Treat dermal irritation or burns with standard topical therapy. Patients developing dermal hypersensitivity reactions may require treatment with systemic or topical corticosteroids or antihistamines.

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- The minimal toxic or lethal dose is variable and not well defined. Toxic effects following inhalation exposure depend on air concentration, time of exposure and underlying diseases.
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Animal Toxicity Studies:

Evidence for Carcinogenicity:

CLASSIFICATION: D; not classifiable as to human carcinogenicity. BASIS FOR CLASSIFICATION: Based on no human carcinogenicity data and inadequate animal data. HUMAN CARCINOGENICITY DATA: None. ANIMAL CARCINOGENICITY DATA: Inadequate.
[U.S. Environmental Protection Agency's Integrated Risk Information System (IRIS) on methyl ethyl ketone (78-93-3) Available from: http://www.epa.gov/ngispgm3/iris on the Substance File List as of March 15, 2000]**PEER REVIEWED**

Non-Human Toxicity Excerpts:

THE SINGLE DOSE ORAL TOXICITY ... HAS BEEN DETERMINED TO BE 3.3 G/KG ... FOR RATS. MASSIVE DOSES MAY BE EXPECTED TO RESULT IN IRRITATION OF THE LUNG & ... /CNS DEPRESSION/.
[Patty, F. (ed.). Industrial Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New York: Interscience Publishers, 1963. 1732]**PEER REVIEWED**

Guinea pigs exposed to 3300 ppm for 13.5 hr showed no signs of intoxication. Exposure to 10,000 ppm for a similar period produced irritation of the eyes and nose within 4 min and /CNS depression/ between 4-5 hr. Exposure to 33,000 ppm for 200 min produced /CNS depression/ and death. Exposure to 100,000 ppm for 45-55 min produced /CNS depression/ after 10 min.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1753]**PEER REVIEWED**

Exposure /of rats/ to 2000 ppm /for 2 hr/ showed no apparent toxicity. Exposure to 8000 ppm killed 3 of 6 rats in 8 hr, while 16,000 ppm for 1 hr caused death of all the animals.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1753]**PEER REVIEWED**

EXPOSURE TO 1500 PPM OF **METHYL ETHYL KETONE (**MEK) ALONE FOR 7-9 WK DID NOT CAUSE PARALYSIS BUT DID ELEVATE PLASMA CHOLINESTERASE LEVELS IN MICE, RATS, & CHICKENS.
[COURI D ET AL; PROC ANNU CONF ENVIRON TOXICOL, 5TH, AMRL-TR-74-125: 109 (1974)]**PEER REVIEWED**

ANALYSIS OF PORPHYRIN CONTENT OF MURINE ERYTHROLEUKEMIA (MEL) CELLS INCUBATED WITH 2-**BUTANONE** SHOWED THAT INCR HEMOGLOBIN SYNTH WAS ACCOMPANIED BY ACCUM OF PORPHYRINS.

[EBERT PS ET AL; CHEM BIOL INTERACT 36 (1): 61 (1981)]**PEER REVIEWED**

The effects of the solvents n-hexane, **butanone** (**methyl ethyl ketone,** MEK) and a mixture of both in the intrapulmonary nerve system of rats were studied by light and electron microscopy. The alteration in the fine structures of the tissues consisted in a disseminated swelling of axons due to a striking multiplication of neurofilaments. Nonspecific axonal alterations could be demonstrated as well. The latter consisted in clusters of phospholipid material within the axoplasm of nerve fibers and the cytoplasm of Schwann cells plus an accumulation of glycogen granules in the axoplasm. Additionally, single degenerative changes of Schwann cells were observed.
[Schmidt R; Respiration 46 (4): 62-9 (1984)]**PEER REVIEWED**

METHYL ETHYL KETONE DELAYED MATCH-TO-SAMPLE DISCRIMINATION TASK IN THE JUVENILE BABOON & ALSO SLOWED RESPONSE TIMES & INCR EXTRA RESPONSES.
[GELLER I; NEUROBEHAV TOXICOL 1 (SUPPL 1): 9 (1979)]**PEER REVIEWED**

METHYL ETHYL KETONE WAS EVALUATED FOR EFFECTS ON A DELAYED MATCH TO SAMPLE DISCRIMINATION TASK IN THE JUVENILE BABOONS. THE ANIMALS WERE EXPOSED TO HALF THE THRESHOLD LIMIT VALUE (245 MG/CU M) FOR 24 HR PER DAY DURING A 7 DAY PERIOD. EACH EXPOSURE CONDITION AFFECTED ACCURACY OF PERFORMANCE MINIMALLY BUT RESULTED IN INCREASED AND DECREASED EXTRA RESPONSES DURING THE DELAY INTERVALS.
[GELLER I; PHARMACOL BIOCHEM BEHAV 11 (4): 401-6 (1979)]**PEER REVIEWED**

Intraperitoneal injection of 750, 1500 or 2000 mg/kg **methyl ethyl ketone** to guinea pigs resulted in elevated serum ornithine carbamyl transferase (OCT) activity at the highest dose, where one of four animals died, and deposition of lipids in the liver with either 1500 or 2000 mg/kg was found.
[DiVincenzo GD et al; Am Ind Hyg Assoc J 34: 329 (1974)]**PEER REVIEWED**

Incubation of Ehrlich-Landschutz diploid ascites tumor cells in media containing 50 and 100 ppm **methyl ethyl ketone** resulted in the destruction of 10.5 and 14.0% of the cells. Control incubations lost only 4.2% of cells in the 5 hr period.
[Holmberg; Environ Res 7: 183 (1974)]**PEER REVIEWED**

Mutagenicity screening in Escherichia coli WP2, and Salmonella typhimurium strains TA1535, TA1537, TA1536 and TA1538 was negative.
[Smirasu Y; J Environ Poll Control 12: 407 (1976)]**PEER REVIEWED**

Pregnant rats inhaled 0, 400, 1000, or 3000 ppm of **methyl ethyl ketone** for 7 hr/day on days 6-15 of gestation. Maternal toxicity evidenced by decreased weight gain and increased water consumption was seen among rats exposed to 3000 ppm. Fetotoxicity (increased incidence of 2 minor skeletal variants) was observed among litters of rats exposed to 3000 ppm.
[Deacon MM et al; Toxicol Appl Pharmacol 59 (3): 620-2 (1981)]**PEER REVIEWED**

Groups of rats were exposed to 100 ppm hexane, 200 ppm **methyl ethyl ketone (**MEK), or fresh air in an exposure chamber 12 hr daily for 24 weeks. Body weight, motor nerve conduction velocity, distal motor

latency, and mixed conduction velocities were measured before exposure and after 4, 8, 12, 16, 20, and 24 wk exposure. ... Exposure to 200 ppm MEK significantly increased motor nerve conduction velocity, and mixed conduction velocities and decreased distal motor latency after 4 week exposure; but at a later stage no significant changes were found. Mixed exposure to 100 ppm hexane and 200 ppm MEK significantly decreased distal motor latency after 4 week exposure and decreased motor nerve conduction velocity and mixed conduction velocities after 20 and 24 week exposure.
[Takeuchi Y et al; Br J Ind Med 40 (2): 199-203 (1983)]**PEER REVIEWED**

Groups of Sprague-Dawley rats were exposed, by inhalation to ... **methyl ethyl ketone (**800 ppm, 2345 mg/cu m) ... for 4 weeks. Increased liver weights and liver-to-body weight ratios were observed. **Methyl ethyl ketone** depressed the formation of 2 metabolites of androstenedione but did not alter the concentration of cytochrome p450 in companion in vitro microsomal metabolism studies.
[Toftgard R et al; Scand J Work Environ Health 7 (1): 31-7 (1981)]**PEER REVIEWED**

Vapors in concn of 1000 ppm or 3000 ppm were embryotoxic and fetotoxic in rats causing acaudia, imperforate anus, and brachygnathia, as well as retardation of fetal development.
[Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984.,p. II-185]**PEER REVIEWED**

Testing of a drop on rabbit eyes indicates moderate reversible injury, graded 5 on a scale of 1-10. The compound was tested externally on the eyes of rabbits, and, according to the degree of injury observed after 24 hours, rated on a scale of 1 to 10. The most severely injurious substances have been rated 10.
[Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986. 617]**PEER REVIEWED**

Male and female Fischer 344 rats were exposed to 0, 1250, 2500, or 5000 ppm **methyl ethyl ketone (**MEK) vapors 6 hr/day, 5 day/wk for 90 days. The 90 day exposures had no adverse effect on the clinical health or growth of male or female rats except for a depression of mean body wt in the 5000 ppm exposure group. The 5000 ppm animals had a slight but significant increase in liver weight, liver weight/body weight ratio, and liver weight/brain weight ratio at necropsy. Serum glutamic-pyruvic transaminase (SGPT) activity in the 2500 ppm female rats was elevated while the 5000 ppm female rats exhibited significantly decreased serum glutamic-pyruvic transaminase SGPT activity. In addition, alkaline phosphatase, potassium, and blood glucose values for the 5000 ppm female rats were increased. ...
[Cavender FL et al; Fundam Appl Toxicol 3: 264-70 (1983)]**PEER REVIEWED**

Chinese hamsters were exposed to ... **methyl ethyl ketone ...** known to be a strong inducer of aneuploidy in the yeast Saccharomyces cerevisiae. ... Solvent yielded negative results in the micro-nucleus test.
[Basler A; Mutat Res 174 (1): 11-13 (1986)]**PEER REVIEWED**

... Cultures of mature organotypic cord ganglia were extracted from fetal mouse spinal cord with the attached dorsal root. MEK at 300 ug/ml nutrient fluid was added to cultures for periods of up to 7 weeks. Cultures were examined under microscope twice weekly for morphological changes and were sampled at 3, 5, and 7 weeks for electron microscopy. Treated cultures remained viable for the 7 week exposure

period. After 6 to 7 weeks of exposure, distinct intraaxonal inclusion occurred along proximal and distal internodes of occasional sensory peripheral nerves (PNS). The structures lengthened and darkened throughout the exposure period and were often associated with axoplasmic granularity. The earliest change in cytoplasm was dispersion of Nissl bodies, which resulted in excessive numbers of free ribosomes or polyribosomal changes. There was a distension of neuronal cisternal systems. By week 5 there were abnormal amounts of smooth or agranular endoplasmic reticulum which appeared swollen with a translucent material. A swollen agranular recticulum was often associated with foci of axoplasmic debris. By week 7, intra-axonal cores of debris and myelin whorls were documented in 25% of the central nervous system and sensory perpipheral nerves axons examined ultrastucturally. ...
[Veronesi B; Neurotoxicology 5 (4): 31-43 (1984)]**PEER REVIEWED**

Chemical test results for cytogenetic effects in Chinese hamster ovary cells ... were negative for both chromosome aberrations and sister chromatid exchanges.
[NTP; Fiscal Year 1987 Annual Plan p.87 (1987) NTP-87-001]**PEER REVIEWED**

An oral dose of 1.5 g/kg to rats resulted in a 63% incr in liver triglycerides after 16 to 23 hr, but did not alter liver histology or incr either of two enzymes, serum glutamic-pyruvic transaminase (alanine transferase (ALT)) and hepatic glucose-6-phosphatase ... Much smaller acute ip doses (0.049 to 0.194 g/kg) to rats appeared not to damage the liver. A single oral dose (15 mmol/kg) of MEK did not affect the hepatobiliary function of rats over an observation period of 10 to 96 hr. ... A graded series of single doses of MEK to guinea-pigs revealed high sensitivity to small changes in dosage. The low dose (0.75 g/kg) appeared to produce no liver damage, whereas 1.5 g/kg produced slight liver damage and 2.0 g/kg produced major liver damage. These results also suggest that guinea-pigs and rats may be equally sensitive to MEK in terms of liver damage even though guinea-pigs survive acute exposure to higher concn of MEK vapor than do rats ... .
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.58 (1993)]**PEER REVIEWED**

Consistent incr in the frequency of food-reinforced lever pressing by rats were detected at MEK exposures as low as 74 mg/cu m (25 ppm) for 2 hr. ... Vestibulo-ocular effects were detected during continuous iv admin of MEK for 1 hr via the caudal vein at a dosage as low as 0.005 g/kg/min ... this dosage is roughly equivalent to inhalation of 2,700 mg/cu m (900 ppm). ... Exposure of mice to 885 mg/cu m (300 ppm) for 30 min did not significantly alter schedule-controlled responses, whereas concn-related suppression of response occurred at consecutive incr concn (for 30 min) ranging from 2,950 to 29,500 mg/cu m (1,000 to 10,000 ppm) ... .
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.67 (1993)]**PEER REVIEWED**

In skin irritation studies, a small dose (8 mg) applied to clipped skin and covered by an impervious plastic film for 24 hr ... produced only minor irritation in male New Zealand albino rabbits. ... A dose of 400 mg applied to the clipped dorsal skin of restrained albino rabbits in a gauze patch produced mild to moderate irritation in some cases. ... Neat MEK (0.1 mL) applied to the clipped skin of the flanks of guinea pigs and rabbits daily for 10 days and left uncovered caused erythema and edema after 24-72 hr. These effects were more marked in rabbits ... .
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.67 (1993)]**PEER REVIEWED**

The results of studies on eye irritation in rabbits are inconsistent. ... 0.005 mL (4 mg) created a severe chemical burn in the rabbit eye, whereas /another/ ... study ... reported less severe irritant effects from the larger dose of 0.1 mL (80 mg). Data from ... /another/ study ... were also inconsistent but indicated that a dose of 0.1 mL (80 mg) produced minimal to moderate eye irritation. Undiluted MEK was used in all three studies ... /however different ocular grading scales were employed/. In all studies irritation disappeared or was markedly reduced by 7 days after treatment. Opaque corneas were apparent following exposure of guinea-pigs to 295,000 mg MEK/cu m (100,000 ppm) for 30 min; recovery from this effect was complete in 4-8 days ... .
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.68 (1993)]**PEER REVIEWED**

Female rats exposed to 14,750 mg/cu m (5,000 ppm) 6 hr/day, 5 days/wk for 90 days showed only slightly incr liver weight, slightly decr brain and spleen weights, and slightly altered blood chemistry in comparison with controls. Male rats receiving this exposure showed only a slightly incr liver weight. At lower concn of MEK (3,688 and 7,375 mg/cu m (1,250 and 2,500 ppm)) there was only slightly incr liver weight for female rats and no significant differences for males in comparison with controls ... . In another subchronic inhalation study ... male and female rats were exposed to MEK concn of 3,700, 7,430 and 14,870 mg/cu m (1,254, 2,518, and 5,041 ppm) 6 hr/day, 5 days/wk for 90 days. No significant effects on food consumption, eyes or nervous system were observed. In addition, MEK-induced morphological changes in the central or peripheral nervous system were detected.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.68 (1993)]**PEER REVIEWED**

In the cat, injection of 150 mg MEK (99.98% pure) per kg, twice a day, 5 days/wk, for up to 8.5 months, into subcutaneous tissue produced abscesses, skin ulceration and generalized weakness but no evidence of damage to the nervous system ... .
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.73 (1993)]**PEER REVIEWED**

... examined the vestibulo-oculomotor reflex (VOR) during iv infusion of MEK into the caudal veins of 18 female Sprague-Dawley rats. The threshold for depression of the VOR was an infusion rate of 70 umol/kg (0.005 g/kg per min) for 1 hr (total dose 30 mg) and the assoc arterial blood level was 1.4 mmol/L. General depression of the central nervous system followed depression of the VOR.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.74 (1993)]**PEER REVIEWED**

... groups of 10 virgin female Swiss CD1 mice and 33 plug-positive (day 0) females were exposed by inhalation on gestation days 6-15 to mean concn of 1174 ... 2980 ... and 8909 ... mg/cu m. ... There was no evidence of maternal toxicity, although there was a slight, treatment-related incr in liver/body weight ratios that was significant at the highest dose level. Mild fetal toxicity was evident at this maternal dose level as a reduction in mean fetal body weight, statistically significant for males. There was no incr in the incidence of intrauterine death, but there was an incr dose-related incidence of misaligned sternebrae, statistically significant at the highest dose level. There were no significant incr in the incidence of malformations, although there were several malformation in one litter (cleft palate, fused ribs, missing vertebrae, syndactyly) in treated groups but not in the control group nor in contemporary control data.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.77 (1993)]**PEER REVIEWED**

... conducted mutagenicity studies on MEK. The test systems comprised the Salmonella/microsome (Ames) assay, the L5178/TK+/- mouse lymphoma (M/L) assay, the BALB/3T3 cell transformation (CT) assay, unscheduled DNA synthesis (UDS) and the micronucleus test. MEK was not found to be genotoxic in these assays.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.80 (1993)]**PEER REVIEWED**

The effect of MEK on the alarm behavior of social insects has been studied. It was considered inactive in producing alarm behavior in the ant Iridomyrmex preinosus ... the harvester ant Pogonomyrmex badius ... and the honeybee Apis Mellifera ... .
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.96 (1993)]**PEER REVIEWED**

The developmental effects observed at an MEK vapor concentration of 3000 ppm were reexamined. Pregnant Sprague-Dawley rats were exposed to 400, 1000, or 3000 ppm of MEK for 7 hr/day on days 6 to 15 of gestation. There were no effects on maternal liver weight; however, a significant decrease in maternal body weight gain was observed in the animals exposed to 3000 ppm of MEK. In addition, none of the exposures affected the pregnancy rate, the number of implantations or fetal resorptions, the litter size, or the fetal body weight. Unlike the initial study, there were no gross or soft-tissue malformations at any exposure level; however, the 3000-ppm exposure caused a significant increase in the incidence of delayed skeletal ossifications (skull and neck) and an increase in the incidence of extra lumbar ribs. /It was/ concluded that MEK was not embryotoxic or teratogenic and only slightly fetotoxic in the rat at exposure concentrations of 3000 ppm.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1759]**PEER REVIEWED**

Groups of pregnant and nonpregnant mice were exposed to MEK vapor concentrations of 400, 1000, or 3000 ppm for 7 hr/day for 10 consecutive days (for pregnant mice, days 6 to 15 of gestation). The nonpregnant and pregnant mice showed no differences in sensitivity to the MEK exposures. The maternal body weight gain, extragestational weight gain, uterine weight, pregnancy rate, and implantation ratio were not affected by exposure to MEK vapors relative to control. The 3000-ppm exposure did, however, result in a relative increase in maternal liver and kidney weight. The percentage of live fetuses, resorptions, and dead fetuses per litter was also unaffected by the treatment. A concentration-related decrease in fetal weight was observed for both the male and females. Although there were no statistically significant increases in the number of malformed fetuses per litter, there were several atypical malformations (cleft palate, fused ribs, missing vertebrae, and syndactyly) not often found in control litters. A statistically significant increase in the incidence of misaligned sternebrae was observed in the fetuses exposed to 3000 ppm of MEK. No developmental or maternal effects were observed at vapor concentrations of 1000 ppm or less. After considering the results from the present study together with results obtained in rats, the authors concluded that MEK vapors caused mild developmental toxicity at concentrations that caused maternal toxicity.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1758]**PEER REVIEWED**

Non-Human Toxicity Values:

LD50 Rat oral 2.9 (95% C.I. 2.3-3.5) g/kg /From table/
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.59 (1993)]**PEER REVIEWED**

LD50 Rat (female) oral 5.52 (95% C.I. 4.50-6.80) g/kg /From table/
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.59 (1993)]**PEER REVIEWED**

LD50 Mouse (male) oral 3.14 + or - 0.67 g/kg /From table/
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.60 (1993)]**PEER REVIEWED**

LC50 (45 min) Mouse (male) inhalation 205,000 + or - 32,500 mg/cu m (69,500 + or - 11,000 ppm) /From table/
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.60 (1993)]**PEER REVIEWED**

LC50 (4 hr) Rat (male) inhalation 34,500 mg/cu m (11,700 ppm) /From table/
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.61 (1993)]**PEER REVIEWED**

LD50 (24 hr) Mouse (male) ip 1.66 + or - 0.74 g/kg /From table/
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.63 (1993)]**PEER REVIEWED**

LD50 (24 hr) Rat (female) ip 1.554 (95% CI 1.229-1.966) g/kg /From table/
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.63 (1993)]**PEER REVIEWED**

LD50 (14 day) Rat (female) ip 0.607 (95% C.I. 0.486-0.748 g/kg /From table/
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.63 (1993)]**PEER REVIEWED**

LD50 (14 days) Rabbit (male) dermal >8 g/kg /From table; 24-hr occluded exposure duration/
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.64 (1993)]**PEER REVIEWED**

Ecotoxicity Values:

LC50 Lepomis macrochirus (bluegill) 5,640-1,690 mg/l 24 to 96-hr /Conditions of bioassay not specified/
[Verschueren, K. Handbook of Environmental Data on Organic Chemicals. 3rd ed. New York, NY: Van Nostrand Reinhold Co., 1996. 1283]**PEER REVIEWED**

LC50 Artemia salina (brine shrimp) 1,950 mg/L 24-hr /From table; bottles not sealed and may have lost MEK during experiment; water pH, temp, and hardness not specified/
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.97 (1993)]**PEER REVIEWED**

LC50 Daphnia magna (water flea) <520 mg/L 48-hr /From table; pH 8 and hardness 173; temp not specified/
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.97 (1993)]**PEER REVIEWED**

LC50 Daphnia magna (water flea) 1382 (95% C.I. 918-3349) mg/l 48-hr /From table; pH 7.21, temp 21.0-23.0 deg C, hardness 38 mg/L calcium carbonate /
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.97 (1993)]**PEER REVIEWED**

LC50 Daphnia magna (water flea) 8890 mg/l 24-hr /From table; pH 7.6-7.7, temp 20-22 deg C, hardness 16 deg (German)/
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.97 (1993)]**PEER REVIEWED**

LC50 Lebistes reticulatus (guppy) 5700 mg/l 24-hr /From table; pH not given, temp 20 deg C, hardness 27.5 mg/L CaCl2/
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.98 (1993)]**PEER REVIEWED**

LC50 Pimephales promelas (fathead minnow) 3200 mg/L 96 hr /From table; pH 7.5, temp 25 deg C, hardness 42.2 mg/L calcium carbonate /
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.99 (1993)]**PEER REVIEWED**

LC50 Lepomis macrochirus (bluegill sunfish) 4467 mg/l 96-hr /From table; pH 7.93, temp 21 deg C, hardness 240 mg/l calcium carbonate /
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.99 (1993)]**PEER REVIEWED**

LC50 Gambusia affinis (mosquito fish) 5600 mg/l 96-hr /From table; pH 7.8-8.3, room temp, hardness not specified/
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.99 (1993)]**PEER REVIEWED**

LC50 Carassius auratus (goldfish) >5000 mg/l 24-hr /From table; pH 7.0, temp 20 deg C, hardness 100 mg/l/
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.99 (1993)]**PEER REVIEWED**

TSCA Test Submissions:

The ability of **methyl ethyl ketone** to induce morphological transformation in the BALB/3T3 mouse cell line (Cell Transformation Assay) was evaluated both in the presence and absence of added metabolic activation by Aroclor-induced rat liver S9 fraction. Based on preliminary clonal toxicity determinations (exposure time=2 hrs), **methyl ethyl ketone,** diluted with phosphate buffered saline, was tested at 18, 13 and 9ul/ml in the absence of metabolic activation, with cell survival ranging from 93.3% to 51.1% relative to the solvent control. Assays with metabolic activation were tested at 10, 8 and 6ul/ml (exposure time=2 hrs), with cell survival ranging from 85.7% to 67.3%. None of the tested concentrations produced

significantly greater transformation frequencies (p > 0.05, Modified Poisson Distribution) relative to the solvent control.
[Microbiological Associates Inc.; Activity of Methyl Ethyl Ketone in the Morphological Transformation Assay using BALB/3T3 Mouse Embryo Cells, Final Report, (1984), EPA Document No. 40-8444072, EPA Fiche No. OTS0507470] **UNREVIEWED**

An inhalation teratology study was conducted with pregnant Sprague-Dawley rats (25/group) receiving whole body exposure to **methyl ethyl ketone** in a dynamic air flow chamber, 7 hours/day on days 6 through 15 of gestation. There was no effect of treatment for all animals as indicated by clinical observations, absolute or relative liver weights, food consumption, number of pregnancies, and mortality. Maternal toxicity was evident by statistical differences between high dose groups and controls for: maternal body weights, maternal body weight gain and water consumption. The average number of live fetuses per litter, incidence of resorption rates, fetal body weight or crown-rump length were not significantly affected by treatment. Significant differences were observed between the fetuses of the control and high dose group for skeletal variations, but no significant external or soft-tissue alterations were observed in any of the fetuses of treated females.
[Dow Toxicology Research Laboratory; Teratologic Evaluation of Inhaled Methyl Ethyl Ketone in Rats, (1979), EPA Document No. 878210652, Fiche No. OTS0206178] **UNREVIEWED**

The ability of **methyl ethyl ketone** to induce specific locus mutations at the TK locus in cultured L5178Y mouse lymphoma cells (Mouse Lymphoma Mutagenicity Assay) was evaluated in the presence and absence of Aroclor-induced rat liver S9 metabolic activation. Based on preliminary toxicity tests, 10 nonactivated cultures treated with 12, 8.9, 6.7, 5.0, 3.8, 2.8, 2.1, 1.6, 1.2 and 0.89ul/ml were cloned, producing a range of 46 - 122% total growth. Ten S9-activated cultures treated with 8.9, 6.7, 5.0, 3.8, 2.8, 2.1, 1.6, 1.2, 0.89 and 0.67ul/ml were cloned, producing a range of 30 - 116% total growth. None of the cultures that were cloned produced mutant frequencies which were significantly greater than the mean mutant frequency of the solvent controls (DMSO, acetone).
[Microbiological Associates Inc.; L5178Y TK +/- Mouse Lymphoma Mutagenicity Assay, Final Report, (1984), EPA Document No. 40-8444072, Fiche No. OTS0507470] **UNREVIEWED**

The mutagenicity of **methyl ethyl ketone** was evaluated in Salmonella tester strains TA98, TA100, TA1535, TA1537 and TA1538 (Ames Test), both in the presence and absence of added metabolic activation by Aroclor-induced rat liver S9 fraction. Based on the results of the preliminary bacterial toxicity determinations, **methyl ethyl ketone,** diluted with DMSO, was tested for mutagenicity at concentrations up to 32 ul/plate (presence metabolic activation) and 16 ul/plate (absence metabolic activation) using the preincubation technique. **Methyl ethyl ketone** did not cause a reproducible positive response in any of the bacterial tester strains, either with or without metabolic activation.
[Microbiological Associates, Inc.; Salmonella/Mammalian-Microsome Preincubation Mutagenicity Assay (Ames Test), (1984), EPA Document No. 40-8444072, Fiche No. OTS0507470] **UNREVIEWED**

The mutagenicity of **methyl ethyl ketone (**MEK) was evaluated in bacterial tester strains E. coli WP2 and WP2uvrA and Salmonella TA98, TA100, TA1535, TA1537 and TA1538, and the yeast Saccharomyces cerevisiae tester strain JD1, both in the presence and absence of added metabolic

activation by Aroclor-induced rat liver S9 fraction. Based on preliminary bacterial toxicity determinations, MEK, diluted with DMSO, was tested for mutagenicity at concentrations up to 4000 ug/plate in the bacterial tests and 5000 ug/plate in the yeast tests using the agar overlay method. MEK did not cause a positive response in any of the bacterial tester strains, either with or without metabolic activation.
[Shell Sittingbourne Research Centre; Toxicity Studies with Chemical Solvents: Short-Term in Vitro Tests for Genotoxic Activity with Methyl Ethyl Ketone. (1982), EPA Document No. 878210125, Fiche No. OTS0206206] **UNREVIEWED**

Methyl ethyl ketone was evaluated for the ability to increase the incidence of micronucleated polychromatic erythrocytes in bone marrow of male and female CD-1 mice treated by single i.p. injection (Micronucleus Test). Groups of 10 mice (5 male, 5 female) were sacrificed 12, 24 and 48 hours following injection of **methyl ethyl ketone** in corn oil at a dose of 1.96 ml/kg body weight (calculated LD20 dose). The ratio of normochromatic to polychromatic erythrocytes were not significantly different ($p > 0.05$, ANOVA) in the treated groups compared with vehicle controls, regardless of sacrifice time. The incidence of micronucleated polychromatic erythrocytes was increased above the vehicle control 24 hours after administration, but was not considered statistically significant when compared to all treatment and vehicle control groups regardless of sacrifice time ($p > 0.05$, ANOVA).
[Microbiological Associates Inc.; Activity of Methyl Ethyl Ketone in the Micronucleus Cytogenetic Assay in Mice, Final Report, (1984), EPA Document No. 40-8444072, Fiche No. OTS0507470] **UNREVIEWED**

The effects of **methyl ethyl ketone** were examined in the rat hepatocyte primary culture/DNA repair assay. Based on preliminary toxicity tests, **methyl ethyl ketone** was tested at concentrations of 5.0 (relative toxicity 74.67%), 2.5, 1.0, 0.5, 0.1 or 0.01 ul/ml (relative toxicity 6.67%). None of the tested concentrations caused a significant increase in unscheduled DNA synthesis over the solvent control (DMSO).
[Microbiological Associates Inc.; Unscheduled DNA Synthesis in Rat Primary Hepatocytes, Final Report, (1984), EPA Document No. 40-8444072, Fiche No. OTS0507470] **UNREVIEWED**

The ability of **methyl ethyl ketone** to cause chromosome aberrations was evaluated in cultured rat (strain not reported) liver cell line. Based on preliminary toxicity determinations, rat liver cultures were exposed to 250, 500 or 1000 ug/ml and incubated for 24 hours. Two hours prior to the end of incubation, colcemid was added and at the end of incubation period 100 cells from each culture were analyzed. No increase (statistical analysis not reported) in the frequency of chromatid gaps, chromatid breaks or total chromatid aberrations were observed in any of the cultures.
[Sittingbourn Research Center; Toxicity Studies with Chemical Solvents: Short Term In Vitro Tests for Genotoxic Activity with Methyl Ethyl Ketone, (1982), EPA Document No. 878210125, Fiche No. OTS0206206] **UNREVIEWED**

METHYL ETHYL KETONE

CASRN: 78-93-3

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Non-Human Toxicity Excerpts:

THE SINGLE DOSE ORAL TOXICITY ... HAS BEEN DETERMINED TO BE 3.3 G/KG ... FOR RATS. MASSIVE DOSES MAY BE EXPECTED TO RESULT IN IRRITATION OF THE LUNG & ... /CNS DEPRESSION/.

[Patty, F. (ed.). Industrial Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New York: Interscience Publishers, 1963. 1732]**PEER REVIEWED**

Guinea pigs exposed to 3300 ppm for 13.5 hr showed no signs of intoxication. Exposure to 10,000 ppm for a similar period produced irritation of the eyes and nose within 4 min and /CNS depression/ between 4-5 hr. Exposure to 33,000 ppm for 200 min produced /CNS depression/ and death. Exposure to 100,000 ppm for 45-55 min produced /CNS depression/ after 10 min.

[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1753]**PEER REVIEWED**

Exposure /of rats/ to 2000 ppm /for 2 hr/ showed no apparent toxicity. Exposure to 8000 ppm killed 3 of 6 rats in 8 hr, while 16,000 ppm for 1 hr caused death of all the animals.

[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1753]**PEER REVIEWED**

EXPOSURE TO 1500 PPM OF **METHYL ETHYL KETONE (**MEK) ALONE FOR 7-9 WK DID NOT CAUSE PARALYSIS BUT DID ELEVATE PLASMA CHOLINESTERASE LEVELS IN MICE, RATS, & CHICKENS.

[COURI D ET AL; PROC ANNU CONF ENVIRON TOXICOL, 5TH, AMRL-TR-74-125: 109 (1974)]**PEER REVIEWED**

ANALYSIS OF PORPHYRIN CONTENT OF MURINE ERYTHROLEUKEMIA (MEL) CELLS INCUBATED WITH 2-**BUTANONE** SHOWED THAT INCR HEMOGLOBIN SYNTH WAS ACCOMPANIED BY ACCUM OF PORPHYRINS.

[EBERT PS ET AL; CHEM BIOL INTERACT 36 (1): 61 (1981)]**PEER REVIEWED**

The effects of the solvents n-hexane, **butanone** (**methyl ethyl ketone,** MEK) and a mixture of both in the intrapulmonary nerve system of rats were studied by light and electron microscopy. The alteration in the fine structures of the tissues consisted in a disseminated swelling of axons due to a striking multiplication of neurofilaments. Nonspecific axonal alterations could be demonstrated as well. The latter consisted in clusters of phospholipid material within the axoplasm of nerve fibers and the cytoplasm of Schwann cells plus an accumulation of glycogen granules in the axoplasm. Additionally, single degenerative changes of Schwann cells were observed.

[Schmidt R; Respiration 46 (4): 62-9 (1984)]**PEER REVIEWED**

METHYL ETHYL KETONE DELAYED MATCH-TO-SAMPLE DISCRIMINATION TASK IN THE JUVENILE BABOON & ALSO SLOWED RESPONSE TIMES & INCR EXTRA RESPONSES.
[GELLER I; NEUROBEHAV TOXICOL 1 (SUPPL 1): 9 (1979)]**PEER REVIEWED**

METHYL ETHYL KETONE WAS EVALUATED FOR EFFECTS ON A DELAYED MATCH TO SAMPLE DISCRIMINATION TASK IN THE JUVENILE BABOONS. THE ANIMALS WERE EXPOSED TO HALF THE THRESHOLD LIMIT VALUE (245 MG/CU M) FOR 24 HR PER DAY DURING A 7 DAY PERIOD. EACH EXPOSURE CONDITION AFFECTED ACCURACY OF PERFORMANCE MINIMALLY BUT RESULTED IN INCREASED AND DECREASED EXTRA RESPONSES DURING THE DELAY INTERVALS.
[GELLER I; PHARMACOL BIOCHEM BEHAV 11 (4): 401-6 (1979)]**PEER REVIEWED**

Intraperitoneal injection of 750, 1500 or 2000 mg/kg **methyl ethyl ketone** to guinea pigs resulted in elevated serum ornithine carbamyl transferase (OCT) activity at the highest dose, where one of four animals died, and deposition of lipids in the liver with either 1500 or 2000 mg/kg was found.
[DiVincenzo GD et al; Am Ind Hyg Assoc J 34: 329 (1974)]**PEER REVIEWED**

Incubation of Ehrlich-Landschutz diploid ascites tumor cells in media containing 50 and 100 ppm **methyl ethyl ketone** resulted in the destruction of 10.5 and 14.0% of the cells. Control incubations lost only 4.2% of cells in the 5 hr period.
[Holmberg; Environ Res 7: 183 (1974)]**PEER REVIEWED**

Mutagenicity screening in Escherichia coli WP2, and Salmonella typhimurium strains TA1535, TA1537, TA1536 and TA1538 was negative.
[Smirasu Y; J Environ Poll Control 12: 407 (1976)]**PEER REVIEWED**

Pregnant rats inhaled 0, 400, 1000, or 3000 ppm of **methyl ethyl ketone** for 7 hr/day on days 6-15 of gestation. Maternal toxicity evidenced by decreased weight gain and increased water consumption was seen among rats exposed to 3000 ppm. Fetotoxicity (increased incidence of 2 minor skeletal variants) was observed among litters of rats exposed to 3000 ppm.
[Deacon MM et al; Toxicol Appl Pharmacol 59 (3): 620-2 (1981)]**PEER REVIEWED**

Groups of rats were exposed to 100 ppm hexane, 200 ppm **methyl ethyl ketone (**MEK), or fresh air in an exposure chamber 12 hr daily for 24 weeks. Body weight, motor nerve conduction velocity, distal motor latency, and mixed conduction velocities were measured before exposure and after 4, 8, 12, 16, 20, and 24 wk exposure. ... Exposure to 200 ppm MEK significantly increased motor nerve conduction velocity, and mixed conduction velocities and decreased distal motor latency after 4 week exposure; but at a later stage no significant changes were found. Mixed exposure to 100 ppm hexane and 200 ppm MEK significantly decreased distal motor latency after 4 week exposure and decreased motor nerve conduction velocity and mixed conduction velocities after 20 and 24 week exposure.
[Takeuchi Y et al; Br J Ind Med 40 (2): 199-203 (1983)]**PEER REVIEWED**

Groups of Sprague-Dawley rats were exposed, by inhalation to ... **methyl ethyl ketone (**800 ppm, 2345 mg/cu m) ... for 4 weeks. Increased liver weights and liver-to-body weight ratios were observed. **Methyl**

ethyl ketone depressed the formation of 2 metabolites of androstenedione but did not alter the concentration of cytochrome p450 in companion in vitro microsomal metabolism studies.
[Toftgard R et al; Scand J Work Environ Health 7 (1): 31-7 (1981)]**PEER REVIEWED**

Vapors in concn of 1000 ppm or 3000 ppm were embryotoxic and fetotoxic in rats causing acaudia, imperforate anus, and brachygnathia, as well as retardation of fetal development.
[Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984.,p. II-185]**PEER REVIEWED**

Testing of a drop on rabbit eyes indicates moderate reversible injury, graded 5 on a scale of 1-10. The compound was tested externally on the eyes of rabbits, and, according to the degree of injury observed after 24 hours, rated on a scale of 1 to 10. The most severely injurious substances have been rated 10.
[Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986. 617]**PEER REVIEWED**

Male and female Fischer 344 rats were exposed to 0, 1250, 2500, or 5000 ppm **methyl ethyl ketone (**MEK) vapors 6 hr/day, 5 day/wk for 90 days. The 90 day exposures had no adverse effect on the clinical health or growth of male or female rats except for a depression of mean body wt in the 5000 ppm exposure group. The 5000 ppm animals had a slight but significant increase in liver weight, liver weight/body weight ratio, and liver weight/brain weight ratio at necropsy. Serum glutamic-pyruvic transaminase (SGPT) activity in the 2500 ppm female rats was elevated while the 5000 ppm female rats exhibited significantly decreased serum glutamic-pyruvic transaminase SGPT activity. In addition, alkaline phosphatase, potassium, and blood glucose values for the 5000 ppm female rats were increased. ...
[Cavender FL et al; Fundam Appl Toxicol 3: 264-70 (1983)]**PEER REVIEWED**

Chinese hamsters were exposed to ... **methyl ethyl ketone ...** known to be a strong inducer of aneuploidy in the yeast Saccharomyces cerevisiae. ... Solvent yielded negative results in the micro-nucleus test.
[Basler A; Mutat Res 174 (1): 11-13 (1986)]**PEER REVIEWED**

... Cultures of mature organotypic cord ganglia were extracted from fetal mouse spinal cord with the attached dorsal root. MEK at 300 ug/ml nutrient fluid was added to cultures for periods of up to 7 weeks. Cultures were examined under microscope twice weekly for morphological changes and were sampled at 3, 5, and 7 weeks for electron microscopy. Treated cultures remained viable for the 7 week exposure period. After 6 to 7 weeks of exposure, distinct intraaxonal inclusion occurred along proximal and distal internodes of occasional sensory peripheral nerves (PNS). The structures lengthened and darkened throughout the exposure period and were often associated with axoplasmic granularity. The earliest change in cytoplasm was dispersion of Nissl bodies, which resulted in excessive numbers of free ribosomes or polyribosomal changes. There was a distension of neuronal cisternal systems. By week 5 there were abnormal amounts of smooth or agranular endoplasmic reticulum which appeared swollen with a translucent material. A swollen agranular recticulum was often associated with foci of axoplasmic debris. By week 7, intra-axonal cores of debris and myelin whorls were documented in 25% of the central nervous system and sensory perpipheral nerves axons examined ultrastucturally. ...
[Veronesi B; Neurotoxicology 5 (4): 31-43 (1984)]**PEER REVIEWED**

Chemical test results for cytogenetic effects in Chinese hamster ovary cells ... were negative for both chromosome aberrations and sister chromatid exchanges.
[NTP; Fiscal Year 1987 Annual Plan p.87 (1987) NTP-87-001]**PEER REVIEWED**

An oral dose of 1.5 g/kg to rats resulted in a 63% incr in liver triglycerides after 16 to 23 hr, but did not alter liver histology or incr either of two enzymes, serum glutamic-pyruvic transaminase (alanine transferase (ALT)) and hepatic glucose-6-phosphatase ... Much smaller acute ip doses (0.049 to 0.194 g/kg) to rats appeared not to damage the liver. A single oral dose (15 mmol/kg) of MEK did not affect the hepatobiliary function of rats over an observation period of 10 to 96 hr. ... A graded series of single doses of MEK to guinea-pigs revealed high sensitivity to small changes in dosage. The low dose (0.75 g/kg) appeared to produce no liver damage, whereas 1.5 g/kg produced slight liver damage and 2.0 g/kg produced major liver damage. These results also suggest that guinea-pigs and rats may be equally sensitive to MEK in terms of liver damage even though guinea-pigs survive acute exposure to higher concn of MEK vapor than do rats ... .
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.58 (1993)]**PEER REVIEWED**

Consistent incr in the frequency of food-reinforced lever pressing by rats were detected at MEK exposures as low as 74 mg/cu m (25 ppm) for 2 hr. ... Vestibulo-ocular effects were detected during continuous iv admin of MEK for 1 hr via the caudal vein at a dosage as low as 0.005 g/kg/min ... this dosage is roughly equivalent to inhalation of 2,700 mg/cu m (900 ppm). ... Exposure of mice to 885 mg/cu m (300 ppm) for 30 min did not significantly alter schedule-controlled responses, whereas concn-related suppression of response occurred at consecutive incr concn (for 30 min) ranging from 2,950 to 29,500 mg/cu m (1,000 to 10,000 ppm) ... .
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.67 (1993)]**PEER REVIEWED**

In skin irritation studies, a small dose (8 mg) applied to clipped skin and covered by an impervious plastic film for 24 hr ... produced only minor irritation in male New Zealand albino rabbits. ... A dose of 400 mg applied to the clipped dorsal skin of restrained albino rabbits in a gauze patch produced mild to moderate irritation in some cases. ... Neat MEK (0.1 mL) applied to the clipped skin of the flanks of guinea pigs and rabbits daily for 10 days and left uncovered caused erythema and edema after 24-72 hr. These effects were more marked in rabbits ... .
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.67 (1993)]**PEER REVIEWED**

The results of studies on eye irritation in rabbits are inconsistent. ... 0.005 mL (4 mg) created a severe chemical burn in the rabbit eye, whereas /another/ ... study ... reported less severe irritant effects from the larger dose of 0.1 mL (80 mg). Data from ... /another/ study ... were also inconsistent but indicated that a dose of 0.1 mL (80 mg) produced minimal to moderate eye irritation. Undiluted MEK was used in all three studies ... /however different ocular grading scales were employed/. In all studies irritation disappeared or was markedly reduced by 7 days after treatment. Opaque corneas were apparent following exposure of guinea-pigs to 295,000 mg MEK/cu m (100,000 ppm) for 30 min; recovery from this effect was complete in 4-8 days ... .
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.68 (1993)]**PEER REVIEWED**

Female rats exposed to 14,750 mg/cu m (5,000 ppm) 6 hr/day, 5 days/wk for 90 days showed only slightly incr liver weight, slightly decr brain and spleen weights, and slightly altered blood chemistry in comparison with controls. Male rats receiving this exposure showed only a slightly incr liver weight. At lower concn of MEK (3,688 and 7,375 mg/cu m (1,250 and 2,500 ppm)) there was only slightly incr liver weight for female rats and no significant differences for males in comparison with controls ... . In another subchronic inhalation study ... male and female rats were exposed to MEK concn of 3,700, 7,430 and 14,870 mg/cu m (1,254, 2,518, and 5,041 ppm) 6 hr/day, 5 days/wk for 90 days. No significant effects on food consumption, eyes or nervous system were observed. In addition, MEK-induced morphological changes in the central or peripheral nervous system were detected.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.68 (1993)]**PEER REVIEWED**

In the cat, injection of 150 mg MEK (99.98% pure) per kg, twice a day, 5 days/wk, for up to 8.5 months, into subcutaneous tissue produced abscesses, skin ulceration and generalized weakness but no evidence of damage to the nervous system ... .
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.73 (1993)]**PEER REVIEWED**

... examined the vestibulo-oculomotor reflex (VOR) during iv infusion of MEK into the caudal veins of 18 female Sprague-Dawley rats. The threshold for depression of the VOR was an infusion rate of 70 umol/kg (0.005 g/kg per min) for 1 hr (total dose 30 mg) and the assoc arterial blood level was 1.4 mmol/L. General depression of the central nervous system followed depression of the VOR.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.74 (1993)]**PEER REVIEWED**

... groups of 10 virgin female Swiss CD1 mice and 33 plug-positive (day 0) females were exposed by inhalation on gestation days 6-15 to mean concn of 1174 ... 2980 ... and 8909 ... mg/cu m. ... There was no evidence of maternal toxicity, although there was a slight, treatment-related incr in liver/body weight ratios that was significant at the highest dose level. Mild fetal toxicity was evident at this maternal dose level as a reduction in mean fetal body weight, statistically significant for males. There was no incr in the incidence of intrauterine death, but there was an incr dose-related incidence of misaligned sternebrae, statistically significant at the highest dose level. There were no significant incr in the incidence of malformations, although there were several malformation in one litter (cleft palate, fused ribs, missing vertebrae, syndactyly) in treated groups but not in the control group nor in contemporary control data.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.77 (1993)]**PEER REVIEWED**

... conducted mutagenicity studies on MEK. The test systems comprised the Salmonella/microsome (Ames) assay, the L5178/TK+/- mouse lymphoma (M/L) assay, the BALB/3T3 cell transformation (CT) assay, unscheduled DNA synthesis (UDS) and the micronucleus test. MEK was not found to be genotoxic in these assays.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.80 (1993)]**PEER REVIEWED**

The effect of MEK on the alarm behavior of social insects has been studied. It was considered inactive in producing alarm behavior in the ant Iridomyrmex preinosus ... the harvester ant Pogonomyrmex badius ... and the honeybee Apis Mellifera ... .

[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.96 (1993)]**PEER REVIEWED**

The developmental effects observed at an MEK vapor concentration of 3000 ppm were reexamined. Pregnant Sprague-Dawley rats were exposed to 400, 1000, or 3000 ppm of MEK for 7 hr/day on days 6 to 15 of gestation. There were no effects on maternal liver weight; however, a significant decrease in maternal body weight gain was observed in the animals exposed to 3000 ppm of MEK. In addition, none of the exposures affected the pregnancy rate, the number of implantations or fetal resorptions, the litter size, or the fetal body weight. Unlike the initial study, there were no gross or soft-tissue malformations at any exposure level; however, the 3000-ppm exposure caused a significant increase in the incidence of delayed skeletal ossifications (skull and neck) and an increase in the incidence of extra lumbar ribs. /It was/ concluded that MEK was not embryotoxic or teratogenic and only slightly fetotoxic in the rat at exposure concentrations of 3000 ppm.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1759]**PEER REVIEWED**

Groups of pregnant and nonpregnant mice were exposed to MEK vapor concentrations of 400, 1000, or 3000 ppm for 7 hr/day for 10 consecutive days (for pregnant mice, days 6 to 15 of gestation). The nonpregnant and pregnant mice showed no differences in sensitivity to the MEK exposures. The maternal body weight gain, extragestational weight gain, uterine weight, pregnancy rate, and implantation ratio were not affected by exposure to MEK vapors relative to control. The 3000-ppm exposure did, however, result in a relative increase in maternal liver and kidney weight. The percentage of live fetuses, resorptions, and dead fetuses per litter was also unaffected by the treatment. A concentration-related decrease in fetal weight was observed for both the male and females. Although there were no statistically significant increases in the number of malformed fetuses per litter, there were several atypical malformations (cleft palate, fused ribs, missing vertebrae, and syndactyly) not often found in control litters. A statistically significant increase in the incidence of misaligned sternebrae was observed in the fetuses exposed to 3000 ppm of MEK. No developmental or maternal effects were observed at vapor concentrations of 1000 ppm or less. After considering the results from the present study together with results obtained in rats, the authors concluded that MEK vapors caused mild developmental toxicity at concentrations that caused maternal toxicity.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1758]**PEER REVIEWED**

METHYL ETHYL KETONE

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Non-Human Toxicity Values:

LD50 Rat oral 2.9 (95% C.I. 2.3-3.5) g/kg /From table/
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.59 (1993)]**PEER REVIEWED**

LD50 Rat (female) oral 5.52 (95% C.I. 4.50-6.80) g/kg /From table/
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.59 (1993)]**PEER REVIEWED**

LD50 Mouse (male) oral 3.14 + or - 0.67 g/kg /From table/
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.60 (1993)]**PEER REVIEWED**

LC50 (45 min) Mouse (male) inhalation 205,000 + or - 32,500 mg/cu m (69,500 + or - 11,000 ppm) /From table/
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.60 (1993)]**PEER REVIEWED**

LC50 (4 hr) Rat (male) inhalation 34,500 mg/cu m (11,700 ppm) /From table/
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.61 (1993)]**PEER REVIEWED**

LD50 (24 hr) Mouse (male) ip 1.66 + or - 0.74 g/kg /From table/
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.63 (1993)]**PEER REVIEWED**

LD50 (24 hr) Rat (female) ip 1.554 (95% CI 1.229-1.966) g/kg /From table/
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.63 (1993)]**PEER REVIEWED**

LD50 (14 day) Rat (female) ip 0.607 (95% C.I. 0.486-0.748 g/kg /From table/
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.63 (1993)]**PEER REVIEWED**

LD50 (14 days) Rabbit (male) dermal >8 g/kg /From table; 24-hr occluded exposure duration/
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.64 (1993)]**PEER REVIEWED**

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Ecotoxicity Values:

LC50 Lepomis macrochirus (bluegill) 5,640-1,690 mg/l 24 to 96-hr /Conditions of bioassay not specified/
[Verschueren, K. Handbook of Environmental Data on Organic Chemicals. 3rd ed. New York, NY: Van Nostrand Reinhold Co., 1996. 1283]**PEER REVIEWED**

LC50 Artemia salina (brine shrimp) 1,950 mg/L 24-hr /From table; bottles not sealed and may have lost MEK during experiment; water pH, temp, and hardness not specified/
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.97 (1993)]**PEER REVIEWED**

LC50 Daphnia magna (water flea) <520 mg/L 48-hr /From table; pH 8 and hardness 173; temp not specified/
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.97 (1993)]**PEER REVIEWED**

LC50 Daphnia magna (water flea) 1382 (95% C.I. 918-3349) mg/l 48-hr /From table; pH 7.21, temp 21.0-23.0 deg C, hardness 38 mg/L calcium carbonate /
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.97 (1993)]**PEER REVIEWED**

LC50 Daphnia magna (water flea) 8890 mg/l 24-hr /From table; pH 7.6-7.7, temp 20-22 deg C, hardness 16 deg (German)/
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.97 (1993)]**PEER REVIEWED**

LC50 Lebistes reticulatus (guppy) 5700 mg/l 24-hr /From table; pH not given, temp 20 deg C, hardness 27.5 mg/L CaCl2/
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.98 (1993)]**PEER REVIEWED**

LC50 Pimephales promelas (fathead minnow) 3200 mg/L 96 hr /From table; pH 7.5, temp 25 deg C, hardness 42.2 mg/L calcium carbonate /
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.99 (1993)]**PEER REVIEWED**

LC50 Lepomis macrochirus (bluegill sunfish) 4467 mg/l 96-hr /From table; pH 7.93, temp 21 deg C, hardness 240 mg/l calcium carbonate /
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.99 (1993)]**PEER REVIEWED**

LC50 Gambusia affinis (mosquito fish) 5600 mg/l 96-hr /From table; pH 7.8-8.3, room temp, hardness not specified/

[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.99 (1993)]**PEER REVIEWED**

LC50 Carassius auratus (goldfish) >5000 mg/l 24-hr /From table; pH 7.0, temp 20 deg C, hardness 100 mg/l/

[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.99 (1993)]**PEER REVIEWED**

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TSCA Test Submissions:

The ability of **methyl ethyl ketone** to induce morphological transformation in the BALB/3T3 mouse cell line (Cell Transformation Assay) was evaluated both in the presence and absence of added metabolic activation by Aroclor-induced rat liver S9 fraction. Based on preliminary clonal toxicity determinations (exposure time=2 hrs), **methyl ethyl ketone,** diluted with phosphate buffered saline, was tested at 18, 13 and 9ul/ml in the absence of metabolic activation, with cell survival ranging from 93.3% to 51.1% relative to the solvent control. Assays with metabolic activation were tested at 10, 8 and 6ul/ml (exposure time=2 hrs), with cell survival ranging from 85.7% to 67.3%. None of the tested concentrations produced significantly greater transformation frequencies ($p > 0.05$, Modified Poisson Distribution) relative to the solvent control.

[Microbiological Associates Inc.; Activity of Methyl Ethyl Ketone in the Morphological Transformation Assay using BALB/3T3 Mouse Embryo Cells, Final Report, (1984), EPA Document No. 40-8444072, EPA Fiche No. OTS0507470] **UNREVIEWED**

An inhalation teratology study was conducted with pregnant Sprague-Dawley rats (25/group) receiving whole body exposure to **methyl ethyl ketone** in a dynamic air flow chamber, 7 hours/day on days 6 through 15 of gestation. There was no effect of treatment for all animals as indicated by clinical observations, absolute or relative liver weights, food consumption, number of pregnancies, and mortality. Maternal toxicity was evident by statistical differences between high dose groups and controls for: maternal body weights, maternal body weight gain and water consumption. The average number of live fetuses per litter, incidence of resorption rates, fetal body weight or crown-rump length were not significantly affected by treatment. Significant differences were observed between the fetuses of the control and high dose group for skeletal variations, but no significant external or soft-tissue alterations were observed in any of the fetuses of treated females.

[Dow Toxicology Research Laboratory; Teratologic Evaluation of Inhaled Methyl Ethyl Ketone in Rats, (1979), EPA Document No. 878210652, Fiche No. OTS0206178] **UNREVIEWED**

The ability of **methyl ethyl ketone** to induce specific locus mutations at the TK locus in cultured L5178Y mouse lymphoma cells (Mouse Lymphoma Mutagenicity Assay) was evaluated in the presence and absence of Aroclor-induced rat liver S9 metabolic activation. Based on preliminary toxicity tests, 10 nonactivated cultures treated with 12, 8.9, 6.7, 5.0, 3.8, 2.8, 2.1, 1.6, 1.2 and 0.89ul/ml were cloned, producing a range of 46 - 122% total growth. Ten S9-activated cultures treated with 8.9, 6.7, 5.0, 3.8, 2.8, 2.1, 1.6, 1.2, 0.89 and 0.67ul/ml were cloned, producing a range of 30 - 116% total growth. None of the cultures that were cloned produced mutant frequencies which were significantly greater than the mean mutant frequency of the solvent controls (DMSO, acetone).

[Microbiological Associates Inc.; L5178Y TK +/- Mouse Lymphoma Mutagenicity Assay, Final Report, (1984), EPA Document No. 40-8444072, Fiche No. OTS0507470] **UNREVIEWED**

The mutagenicity of **methyl ethyl ketone** was evaluated in Salmonella tester strains TA98, TA100,

TA1535, TA1537 and TA1538 (Ames Test), both in the presence and absence of added metabolic activation by Aroclor-induced rat liver S9 fraction. Based on the results of the preliminary bacterial toxicity determinations, **methyl ethyl ketone,** diluted with DMSO, was tested for mutagenicity at concentrations up to 32 ul/plate (presence metabolic activation) and 16 ul/plate (absence metabolic activation) using the preincubation technique. **Methyl ethyl ketone** did not cause a reproducible positive response in any of the bacterial tester strains, either with or without metabolic activation.
[Microbiological Associates, Inc.; Salmonella/Mammalian-Microsome Preincubation Mutagenicity Assay (Ames Test), (1984), EPA Document No. 40-8444072, Fiche No. OTS0507470] **UNREVIEWED**

The mutagenicity of **methyl ethyl ketone (**MEK) was evaluated in bacterial tester strains E. coli WP2 and WP2uvrA and Salmonella TA98, TA100, TA1535, TA1537 and TA1538, and the yeast Saccharomyces cerevisiae tester strain JD1, both in the presence and absence of added metabolic activation by Aroclor-induced rat liver S9 fraction. Based on preliminary bacterial toxicity determinations, MEK, diluted with DMSO, was tested for mutagenicity at concentrations up to 4000 ug/plate in the bacterial tests and 5000 ug/plate in the yeast tests using the agar overlay method. MEK did not cause a positive response in any of the bacterial tester strains, either with or without metabolic activation.
[Shell Sittingbourne Research Centre; Toxicity Studies with Chemical Solvents: Short-Term in Vitro Tests for Genotoxic Activity with Methyl Ethyl Ketone. (1982), EPA Document No. 878210125, Fiche No. OTS0206206] **UNREVIEWED**

Methyl ethyl ketone was evaluated for the ability to increase the incidence of micronucleated polychromatic erythrocytes in bone marrow of male and female CD-1 mice treated by single i.p. injection (Micronucleus Test). Groups of 10 mice (5 male, 5 female) were sacrificed 12, 24 and 48 hours following injection of **methyl ethyl ketone** in corn oil at a dose of 1.96 ml/kg body weight (calculated LD20 dose). The ratio of normochromatic to polychromatic erythrocytes were not significantly different ($p > 0.05$, ANOVA) in the treated groups compared with vehicle controls, regardless of sacrifice time. The incidence of micronucleated polychromatic erythrocytes was increased above the vehicle control 24 hours after administration, but was not considered statistically significant when compared to all treatment and vehicle control groups regardless of sacrifice time ($p > 0.05$, ANOVA).
[Microbiological Associates Inc.; Activity of Methyl Ethyl Ketone in the Micronucleus Cytogenetic Assay in Mice, Final Report, (1984), EPA Document No. 40-8444072, Fiche No. OTS0507470] **UNREVIEWED**

The effects of **methyl ethyl ketone** were examined in the rat hepatocyte primary culture/DNA repair assay. Based on preliminary toxicity tests, **methyl ethyl ketone** was tested at concentrations of 5.0 (relative toxicity 74.67%), 2.5, 1.0, 0.5, 0.1 or 0.01 ul/ml (relative toxicity 6.67%). None of the tested concentrations caused a significant increase in unscheduled DNA synthesis over the solvent control (DMSO).
[Microbiological Associates Inc.; Unscheduled DNA Synthesis in Rat Primary Hepatocytes, Final Report, (1984), EPA Document No. 40-8444072, Fiche No. OTS0507470] **UNREVIEWED**

The ability of **methyl ethyl ketone** to cause chromosome aberrations was evaluated in cultured rat (strain not reported) liver cell line. Based on preliminary toxicity determinations, rat liver cultures were exposed

to 250, 500 or 1000 ug/ml and incubated for 24 hours. Two hours prior to the end of incubation, colcemid was added and at the end of incubation period 100 cells from each culture were analyzed. No increase (statistical analysis not reported) in the frequency of chromatid gaps, chromatid breaks or total chromatid aberrations were observed in any of the cultures.
[Sittingbourn Research Center; Toxicity Studies with Chemical Solvents: Short Term In Vitro Tests for Genotoxic Activity with Methyl Ethyl Ketone, (1982), EPA Document No. 878210125, Fiche No. OTS0206206] **UNREVIEWED**

METHYL ETHYL KETONE

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Metabolism/Pharmacokinetics:

Metabolism/Metabolites:

METHYL ETHYL KETONE (MEK) OCCURS ... IN NORMAL HUMAN URINE & ... HAS POSSIBLE DIETARY ORIGIN; ITS MORE PROBABLE PRECURSOR IS ALPHA-METHYLACETOACETIC ACID. LIKE OTHER KETONES ... MEK IS REDUCED ... IN THE BODY. ONLY 30-40% ... IS ELIMINATED IN EXPIRED AIR ... .
[Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965. 422]**PEER REVIEWED**

IT HAS BEEN SHOWN TO INCREASE THE GLUCURONIC ACID OUTPUT ... & URINE OF RABBITS RECEIVING IT HAS BEEN STATED ... TO CONTAIN THE GLUCURONIDE OF 2-BUTANOL.
[Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965. 422]**PEER REVIEWED**

GUINEA PIGS WERE GIVEN SINGLE 450 MG/KG IP DOSES OF **METHYL ETHYL KETONE (**MEK). MEK PRODUCED 2-BUTANOL, 3-HYDROXY-2-**BUTANONE**, & 2,3-BUTANEDIOL.
[DIVINCENZO GD ET AL; TOXICOL APPL PHARMACOL 36 (3): 511 (1976)]**PEER REVIEWED**

Uptake of oxygen by Mycobacterium smegmatis 442, and Corynebacterium sp during metabolism of 1 ul of **methyl ethyl ketone (**MEK) in Warburg respirometers, was 196 and 266 ul of oxygen respectively.
[Lukins HB, Foster JW; J Bacteriol 85: 1076-87 (1963)]**PEER REVIEWED**

Milk cultures of five Leuconostoc dextranicum strains were capable of reducing **methyl ethyl ketone (**MEK) to 2-butyl alcohol.
[Keenan TW; Appl Microbiol 16: 1881-5 (1968)]**PEER REVIEWED**

Resting cells of Lactobacillus brevis 24 reduced **methyl ethyl ketone (**MEK) quantitatively to 2-butyl alcohol when incubated in phosphate buffer for 24 hr at 30 deg C.
[Keen AR et al; J Dairy Res 41: 249-57 (1974)]**PEER REVIEWED**

Rats were given a single oral dose of **methyl ethyl ketone (**MEK). The blood concn of MEK and metabolites 4 hr after dosing were: MEK (94.1 mg/100 ml); 2-butanol (3.2 mg/100 ml); 3-hydroxy-2-butanol (2.4 mg/100 ml) and 2,3-butanediol (8.6 mg/100 ml). Blood concn of the parent compound and metabolites 18 hr after dosing with MEK were: MEK (6.2 mg/100 ml); 2-butanol (0.6 mg/100 ml); 3-hydroxy-2-**butanone** (1.4 mg/100 ml); and 2,3-butanediol (25.6 mg/100 ml).
[Dietz FKJ, Traiger GJ; Toxicology 14: 209-14 (1979)]**PEER REVIEWED**

MEK has been reported to be a metabolic end product of natural gas (methane 88%, ethane 5%, propane 5%, iso-butane 2%, with traces of t-butyl mercaptan and methyl acrylate) inhaled for 2 hr by ICR mice ... In an in vivo study of the metabolism of propane, n-butane and iso-butane inhaled for 1 hr by ICR mice,

it was found that n-butane gave rise to sec-butanol and MEK ... In vitro studies showed that mouse liver microsomal preparations metabolized n-butane to sec-butanol, the precursor of MEK ... Inhalation by male Sprague-Dawley rats of sec-butanol at concn of 5900 mg/cu m (2000 ppm) for 3 days or 1475 mg/cu m (500 ppm) for 5 days caused marked enzyme induction of cytochrome P-450 in liver and kidney but other butanol isomers did not have this effect ... The authors concluded that the mechanism of induction was via the sec-butanol metabolite MEK.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.51 (1993)]**PEER REVIEWED**

... the toxic effects of MEK and 2-butanol were essentially identical in rats, and that 2-butanol was rapidly oxidized to MEK. ... identified the metabolites of MEK in guinea pigs as 2-butanol, 3-hydroxy-2-**butanone** and 2,3-butanediol. They hypothesized that the metabolism followed both oxidative and reductive pathways, with the latter leading to the production of 2-butanol.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.52 (1993)]**PEER REVIEWED**

In rats exposed by inhalation to 1760 mg MEK/cu m (600 ppm), there were only marginal effects on microsomal cytochrome P-450 activities ... However, a daily dose of 1.4 mL MEK per kg for 3 days incr the amounts of ethanol- and phenobarbital-inducible cytochromes P-450 ...
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.53 (1993)]**PEER REVIEWED**

In a study on male Sprague-Dawley rats, pretreatment with MEK elevated total microsomal cytochrome P-450 and NADPH-dependent cytochrome-c-reductase, the rates of oxidation of N-nitrosodimethylamine, benzphetamine and pentoxyresorufin, and also the levels of immunoreactive protein for both P-450 isozymes ... In a study of hepatotoxicity in rats, ... found that MEK incr liver cytochrome P-450 content (33-86%) and glutathione-S-transferase (GST) activity (42-64%) but had no effect on serum glutamate dehydrogenase (GLDH) activity. ... studied the effects on hepatic cytochrome P-450 activities of repeated daily doses of 1.87 mL/kg given by gavage to male Fischer-344 rats. The activity of 7-ethoxy coumarin-O-deethylase was incr by up to 500% after 1 to 7 days of MEK treatment, but there was practically no change in benzphetamine-N-demethylase activity. In another study in male Sprague-Dawley rats, admin of MEK by gavage cause an incr in hepatic acetanilide hydroxylase and a marginal incr in aminopyrine-N-demethylase activities ... .
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.53 (1993)]**PEER REVIEWED**

MEK has been identified as a minor but normal constituent of urine ... serum and urine of diabetics ... and expired air ... . Its production in the body has been attributed to isoleucine catabolism ... studies ... indicate that the same metabolites are produced and excreted in humans as in experimental animals. ... further indicated that in an inhalation exposure to 590 mg MEK/cu m (200 ppm) the calculated areas under the curves of blood solvent concn versus time (AUC) for MEK and 2,3-butanediol were equal, which suggests that MEK is almost completely transformed to 2,3-butanediol. The bulk of MEK absorbed thus enters the general metabolism and is transformed to simple compounds like carbon dioxide and water.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.55 (1993)]**PEER REVIEWED**

Absorption, Distribution & Excretion:

Measurable (2.54 to 13 ug/l) quantities of **methyl ethyl ketone** appeared in expired air of adult humans 3 min following dermal exposure to 100 ml **methyl ethyl ketone** applied to 91.5 sq cm of skin.
[Wurster; J Pharm Sci 54: 554 (1965)]**PEER REVIEWED**

Ketones are readily absorbed through the intact skin. Usually they are rapidly excreted ... in the expired air. /Ketones/
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 1170]**PEER REVIEWED**

Workers occupationally exposed to **methyl ethyl ketone (**MEK) were examined. ... Workers exposed to 300 micrograms per liter MEK, the aveolar concn was 30% of the environmental concn. Lung uptake averaged 1.05 mg/min. The blood concn of MEK ranged from 842 to 9573 ug/l, with a mean of 2630 ug/l. Blood concn of MEK were strongly correlated with alveolar concn. MEK was more soluble in heart and muscle tissue than in lung tissue or fat. Urinary MEK excretion ranged from 120 to 1120 mg/l, with a mean of 487 mg/l. ... MEK was not persistent in the tissues. ... Urinary excretion of MEK and acetylmethylcarbinol are only around 0.1% of MEK lung absorption, the main pathway through which MEK is eliminated is unknown.
[Perbellini L et al; Intern Arch Occup Environ Health 54 (1): 73-81 (1984)]**PEER REVIEWED**

ALTHOUGH ABSORPTION ... THROUGH THE SKIN MAY OCCUR, IT HAS BEEN SHOWN THAT IT IS LOW IN TOXICITY BY THIS ROUTE.
[Patty, F. (ed.). Industrial Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New York: Interscience Publishers, 1963. 1732]**PEER REVIEWED**

Percutaneous absorption of MEK appears to be rapid ... MEK was present in the exhaled air of human subjects within 2.5-3.0 min after it was applied to normal skin of the forearm, and the concn of MEK in exhaled air reached a plateau in 2-3 hr. The rate of absorption was controlled mainly by the moisture content of the skin. With dry skin, absorption was slow, and it took 4-5 hr for the concn of MEK in expired air to attain a plateau. With moist skin, absorption was very rapid initially. MEK was detected in expired air in measurable concn within 30 sec after an application of MEK to the forearm, and a max concn in expired air, averaging 4X the plateau level for normal and dry skin, was achieved in 10-15 min.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.49 (1993)]**PEER REVIEWED**

The absorption of MEK via the lungs was examined ... in a study of workers exposed in industrial workplace. The MEK concn in alveolar and expired air correlated significantly with the environmental concn, and averaged 30% of the latter. In more recent studies ... values for pulmonary absorption ranging from 41.1% to 55.8% were obtained. ... Deeper inhalation incr the alveolar volume relative to the dead space (the non-alveolar volume of the respiratory system), and thus incr the apparent absorption ... .
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.49 (1993)]**PEER REVIEWED**

Results of studies ... indicated a rapid transfer of MEK vapor into the blood stream. ... the concn of MEK

in the blood and urine were significantly correlated with the environmental concn, indicating rapid transfer to the blood and thence to other tissues. In human volunteer subjects, exercise during exposure markedly incr the MEK level in blood in comparison with sedentary behavior ... indicating that the blood MEK level also depended on the rate of uptake. ... also found significant correlations between environmental levels of MEK and amounts excreted in the urine of exposed workers. The concn of MEK in urine rose from essentially 0 to 70% of its max value during the first 2 hr of an 8-hr shift ... .
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.50 (1993)]**PEER REVIEWED**

... studied biological monitoring of occupational exposure to MEK in 67 healthy male workers employed in plastic bag or video-tape production. Their ages ranged between 18 and 52 yr with an average working experience of 8.6 yr. for the majority of the workers, atmospheric MEK concn were in the range of 30-885 mg/cu m (10-300 ppm). MEK concn in urine, blood and exhaled air were measured once/week at the end of a shift. About 10% of absorbed MEK was eliminated in the exhaled air. Following exposure to 590 mg/cu m (200 ppm), the urinary concn was 5.1 umol/L or 4.11 mg/g creatinine. The correlation coefficients between atmospheric MEK concn and end-of-shift urine, blood and exhaled air were 0.89, 0.85, and 0.79, respectively. The authors also reported good correlation between blood and urinary MEK ... and between blood and exhaled air concn ... but poor correlation between exhaled air and urinary MEK concn.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.50 (1993)]**PEER REVIEWED**

In male rats given a large MEK dose (1505 or 1690 mg/kg) in water, blood concn reached maxima of 0.95 and 0.94 mg/mL 4 hr after ingestion and subsequently declined sharply, indicating protracted absorption of this dose from the GI tract ... .
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.51 (1993)]**PEER REVIEWED**

... intraperitoneal injection of MEK in research on metabolism and toxicity, suggest that absorption from the peritoneal cavity is rapid.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.51 (1993)]**PEER REVIEWED**

The distribution of MEK in human tissues was examined ... in two solvent-exposed workers who died suddenly of heart attacks at the workplace. The results of this study ... indicate that the solubility of MEK is similar for all tissues. ... With a blood/air partition coefficient of 202, MEK can reach equilibrium concn in a compartment in about 3 min. Distribution volumes were 6.0 for vessel-rich tissues, 39.6 for muscle and 12.8 for fat. Biological half-lives for the same tissues were 0.8, 21.8 and 23.3 min, respectively.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.51 (1993)]**PEER REVIEWED**

The results of in vitro measurements at 37 deg C of human tissue-gas partition coefficients, obtained by exposing samples of blood and tissue to a known concn of MEK ... The partition coefficients ranged from 96 to 162, but did not exceed 111, with the exception of whole blood (125), blood plasma (133) and fat (162). Other blood-gas partition coefficients measurements for MEK are 202 ... and 215 ... .
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.51

(1993)]**PEER REVIEWED**

... provided evidence that MEK can enter the liver of rats and guinea-pigs, and ... reported that it can cross the placenta and enter the human fetus.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.51 (1993)]**PEER REVIEWED**

MEK and its metabolites are excreted by the lungs and kidneys. ... only 3% of the calculated absorbed dose during a 4-hr exposure to 590 mg MEK/cu m (200 ppm) was secreted unchanged in the exhaled air of volunteers after the exposure. The fractional elimination of unchanged substance however depends on the efficiency of metabolic clearance. Since metabolic saturation for MEK in humans begins at relatively low levels (about 100 ppm) of exposure ... proportionally greater amounts of MEK would be expected to be excreted via the lungs (and kidneys) at high exposure levels.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.55 (1993)]**PEER REVIEWED**

Relatively little of absorbed MEK is excreted unchanged via the kidneys; a study of occupationally exposed workers revealed that it is less than 0.1% of the alveolar uptake ... In a similar study of workers occupationally exposed to a mixture of solvents, the excretion of MEK and a major recognizable metabolite, 3-hydroxy-2-**butanone**, was 0.1% of alveolar uptake ... The concentrations of both MEK and 3-hydroxy-2-**butanone** in urine were significantly correlated with the environmental level of MEK. Other metabolites of MEK, 2-butanol or 2,3-butanediol ... identified in the serum of guinea pigs, were not detected in the urine of the exposed workers. ... however ... human excretion of 2,3-butanediol was individually variable but averaged 2% of the absorbed MEK. The urinary excretion of 2-butanol, a minor metabolite of MEK was examined ... clearance of 2-butanol admin by gavage in rabbits was about 14% of the admin dose and in the form of a glucuronide.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.55 (1993)]**PEER REVIEWED**

Absorption of methylethylketone is rapid via inhalation and ingestion, and the compound is presumably a moderate skin penetrant as well. Since methylethylketone is both water and lipid soluble, it is rather evenly distributed in tissues.
[Zenz, C., O.B. Dickerson, E.P. Horvath. Occupational Medicine. 3rd ed. St. Louis, MO., 1994 149]**PEER REVIEWED**

Biological Half-Life:

Guinea pigs were given a single dose of **methyl ethyl ketone (**MEK) ip at 450 mg/kg. Blood samples were taken via cardiac puncture at 1, 2, 4, 6, 8, 12 and 16 hr after dosing. Serum half-life of MEK was estimated at 270 minutes.
[Divincenzo GD et al; Toxicol Appl Pharm 36: 511-22 (1976)]**PEER REVIEWED**

... The biological half lives for elimination of acetone and MEK calculated on the basis of a first order kinetic assumption were 3.9 hours and 49 minutes, respectively. ... Workers exposed to acetone or MEK for 6 to 8 hours could expect to have a residual body burden of acetone the next morning, whereas MEK would be essentially eliminated.
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Proceedings of the Third Joint US-Finish Science Symposium p.111-14 (1986)]**PEER REVIEWED**

The distribution of MEK in human tissues was examined ... in two solvent-exposed workers who died suddenly of heart attacks at the workplace. ... Distribution volumes were 6.0 for vessel-rich tissues, 39.6 for muscle and 12.8 for fat. Biological half-lives for the same tissues were 0.8, 21.8 and 23.3 min, respectively.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.51 (1993)]**PEER REVIEWED**

Both animal and human data indicate a rapid turnover of MEK. In guinea-pigs receiving an ip dose of 450 mg MEK/kg, the half-life of MEK in blood serum was 4.5 hr and the clearance time for MEK in serum was 12 hr. For the metabolites 2-butanol, 3-hydroxy-2-**butanone** and 2,3-butanediol, the clearance time in serum was 11 hr ... In a study ... on rats given an oral dose of 2-**butanone** of 2.1 mg/kg, there was a half-life of 3.6 hr for MEK in blood if the rate of loss was assumed to be constant between the two times of measurement (4 and 18 hrs) after dosing. Data from a study ... on rats receiving oral doses of 2-butanol or MEK also indicate a half-life of about 4 hr for MEK. ... the clearance rate for 3-hydroxy-2-**butanone** and 2,3-butanediol was independent of dose for the two doses used (0.4 and 0.8 g/kg) and that the half-lives for these metabolites of MEK were 47 min and 3.45 hr, respectively.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.56 (1993)]**PEER REVIEWED**

... reported a steady incr in blood concn during 4-hr exposures of human volunteer subjects to 590 mg/cu m (200 ppm) and observed a rapid elimination of MEK, with half-lives of 30 min during the first post-exposure hr and 81 min thereafter. An inhalation study with two volunteer subjects exposed to MEK for 4 hr at concn of 74,590 and 1,180 mg/cu m (25,200 and 400 ppm, respectively) indicated that the kinetics of MEK were dose dependent at higher exposure concn, i.e., much higher levels of MEK in blood were reached relative to inhaled concn, and the post-exposure elimination of MEK in blood was slower (zero-order kinetics). Simulated exposure to MEK for 8 hr suggests that saturation kinetics are reached at about 295 mg/cu m (100 ppm) at rest and 148 mg/cu m (50 ppm) during light exercise ... .
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Mechanism of Action:

The effects of the solvents n-hexane, **butanone** (**methyl ethyl ketone,** MEK) and a mixture of both in the intrapulmonary nerve system of rats were studied by light and electron microscopy. The alteration in the fine structures of the tissue consisted in a disseminated swelling of axons due to a striking multiplication of neurofilaments. Nonspecific axonal alterations could be demonstrated as well. The latter consisted in clusters of phospholipid material within the axoplasm of nerve fibers and the cytoplasm of Schwann cells plus an accumulation of glycogen granules in the axoplasm. Additionally, single degenerative changes of Schwann cells were observed. An enzyme associated metabolic damage with a concomitant impairment of axonal flow is discussed as a possible underlying pathomechanism.
[Schmidt R et al; Respiration 46 (4): 362-9 (1984)]**PEER REVIEWED**

There is very limited info on the mechanisms of toxic action of MEK. Relatively high inhaled concn 1,475-29,500 mg/cu m (500-10,000 ppm) caused pulmonary vasoconstriction and hypertension in cats and dogs ... From the toxicological point of view, interactions leading to the potentiation of effects,

particularly neurotoxicity, by other intrinsically toxic substances constitute the main hazard of MEK. The mechanisms underlying these interactions are incompletely known ... .
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.57 (1993)]**PEER REVIEWED**

Interactions:

IT DOES NOT APPEAR TO BE NEUROTOXIC BY ITSELF, IT POTENTIATES NEUROTOXICITY OF OTHER HEXACARBONS; REPORTED IN HUMANS EXPOSED TO **METHYL ETHYL KETONE (**MEK) & N-HEXANE.
[ALTENKIRCH ET AL; J NEUROL 214: 152 (1977)]**PEER REVIEWED**

Methyl ethyl ketone potentiates carbon tetrachloride hepatoxicity in rats. Oral dosing with **methyl ethyl ketone** at 1.87, 2.4, or 1.2 ml/kg followed by ip injection with carbon tetrachloride at 0.1 ml/kg significantly enhanced the hepatotoxicity of carbon tetrachloride as measured by increased serum glutamic pyruvic transaminase activity and hepatic triglyceride concentration and decreased hepatic glucose-6-phosphatase activity.
[Traiger GJ, Bruckner JV; J Pharmacol Exp Ther 196: 493 (1976)]**PEER REVIEWED**

A study of the potential relationship between **methyl ethyl ketone** and 2,5-hexanedione was conducted. Male F344 rats weighing between 200 and 320 g were used. A sensorimotor/behavioral battery consisting of two simple reflex tests, hind limb grasp and hind limb place, and two complex function tests, balance beam and accelerating rotorod performance, was used for identification and quantification of neurological deficits. ... The enhancement of 2,5-hexanedione induced toxicity by **methyl ethyl ketone** could be correlated with higher tissue exposures of 2,5-hexanedione in animals receiving the combined treatment. ... **Methyl ethyl ketone** may compete with 2,5-hexanedione for critical and non-critical binding sites at the target neurofilament proteins.
[Ralston WH et al; Toxicol Appl Pharm 81 (2): 319-27 (1985)]**PEER REVIEWED**

The effects of acute exposure to toluene and **methyl ethyl ketone (**MEK) singly and in combination were investigated. ... The effects of these chemicals on behavior and body burden were determined. ... MEK had no effect on any measures. Behavior performance was not affected by the combination of toluene and MEK. Body burden of the two solvents was not additive. ... Neither chemical potentiated the effect of the other at the concentrations studied.
[Dick RB et al; Int Arch Occup Environ Health 54 (2): 91-109 (1984)]**PEER REVIEWED**

... An important observation was the marked potentiation of peripheral neurotoxicity observed when animals were exposed to n-butyl ketone in combination with **methyl ethyl ketone** at a ratio of 1:5, n-butyl ketone: **methyl ethyl ketone.** The latter solvent showed no neurotoxic effect alone.
[Saida K et al; J Neuropathol Exp Neurol 35 (3): 207-25 (1976)]**PEER REVIEWED**

... The toxic neuropathy induced by **methyl ethyl ketone** is clinically and morphologically identical with that induced by n-hexane and methyl butyl ketone. **Methyl ethyl ketone** can act synergistically with n-hexane to produce toxic neuropathy.

[Alterkirch H et al; J Neurology 214: 137-52 (1977)]**PEER REVIEWED**

Ingestion of ethanol (0.8 g/kg) combined with an inhalation exposure to MEK (590 mg/cu m, 200 ppm) inhibited the oxidative metabolism of MEK and led to a marked incr in the blood concn of MEK ... There was a concurrent, even more pronounced elevation of the blood 2-butanol concn; the most likely explanation is competitive inhibition by ethanol of the oxidation of 2-butanol back to MEK. Ethanol also appeared to interact with the further biotransformation of 2,3-butanediol as the urinary excretion of the metabolite was incr. Co-exposure with xylene, however, had no effect on the human metabolism or rate of elimination of MEK ... .
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.57 (1993)]**PEER REVIEWED**

... found that MEK and certain other polar aprotic solvents were strong inducers of aneuploidy in the yeast. The induction of aneuploidy by MEK was markedly potentiated by coexposure to ethyl acetate ... or with nocodazol ... .
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.80 (1993)]**PEER REVIEWED**

MEK interacts with hexacarbon compounds and potentiates their neurotoxicity ... Potentially MEK co-exposure could affect the metabolism of the hexacarbon compounds or the toxic process by which the hexacarbons induce the neuropathy. ... The metabolic pathway involves hepatic microsomal oxidation to 2,5-hexanedione, the proximate neurotoxicant, which is thought to induce cross-linking of neurofilaments, blockage of transport at the node of Ranvier, and swelling from accumulated neurofilaments proximal to the nodes and axonal degeneration distal to the nodes.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.101 (1993)]**PEER REVIEWED**

Carbon tetrachloride (CCl4), chloroform (CHCl3) and related haloalkane solvents are liver and kidney poisons as well as central nervous depressants ... It has long been known that the hepatotoxic action of CCl4 is potentiated by ethanol, and more recently that the hepatic and/or renal toxicity of CCl4, CHCl3, trichloroethylene, 1,1,2-trichloroethane and related compounds is potentiated by n-hexane, ethanol, isopropanol, acetone, MEK, MBK, 2,5-HD, and other ketones or chemicals that are metabolized to ketones ... Even an incr of naturally occurring ketones in the body via diabetes can precipitate potentiation. Decr the transformation of isopropanol to acetone by the admin of an inhibitor of alcohol dehydrogenase, pyrazole, has reduced potentiation of haloalkane toxicity. Although the phenomenon is referred to as haloalkane toxicity, experimental work in general appears largely or entirely limited to chlorinated compounds, and specific studies on MEK are limited to interactions with CCl4 and CHCl3.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.115 (1993)]**PEER REVIEWED**

METHYL ETHYL KETONE

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Metabolism/Metabolites:

METHYL ETHYL KETONE (MEK) OCCURS ... IN NORMAL HUMAN URINE & ... HAS POSSIBLE DIETARY ORIGIN; ITS MORE PROBABLE PRECURSOR IS ALPHA-METHYLACETOACETIC ACID. LIKE OTHER KETONES ... MEK IS REDUCED ... IN THE BODY. ONLY 30-40% ... IS ELIMINATED IN EXPIRED AIR ... .
[Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965. 422]**PEER REVIEWED**

IT HAS BEEN SHOWN TO INCREASE THE GLUCURONIC ACID OUTPUT ... & URINE OF RABBITS RECEIVING IT HAS BEEN STATED ... TO CONTAIN THE GLUCURONIDE OF 2-BUTANOL.
[Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965. 422]**PEER REVIEWED**

GUINEA PIGS WERE GIVEN SINGLE 450 MG/KG IP DOSES OF **METHYL ETHYL KETONE (**MEK). MEK PRODUCED 2-BUTANOL, 3-HYDROXY-2-**BUTANONE**, & 2,3-BUTANEDIOL.
[DIVINCENZO GD ET AL; TOXICOL APPL PHARMACOL 36 (3): 511 (1976)]**PEER REVIEWED**

Uptake of oxygen by Mycobacterium smegmatis 442, and Corynebacterium sp during metabolism of 1 ul of **methyl ethyl ketone (**MEK) in Warburg respirometers, was 196 and 266 ul of oxygen respectively.
[Lukins HB, Foster JW; J Bacteriol 85: 1076-87 (1963)]**PEER REVIEWED**

Milk cultures of five Leuconostoc dextranicum strains were capable of reducing **methyl ethyl ketone (**MEK) to 2-butyl alcohol.
[Keenan TW; Appl Microbiol 16: 1881-5 (1968)]**PEER REVIEWED**

Resting cells of Lactobacillus brevis 24 reduced **methyl ethyl ketone (**MEK) quantitatively to 2-butyl alcohol when incubated in phosphate buffer for 24 hr at 30 deg C.
[Keen AR et al; J Dairy Res 41: 249-57 (1974)]**PEER REVIEWED**

Rats were given a single oral dose of **methyl ethyl ketone (**MEK). The blood concn of MEK and metabolites 4 hr after dosing were: MEK (94.1 mg/100 ml); 2-butanol (3.2 mg/100 ml); 3-hydroxy-2-butanol (2.4 mg/100 ml) and 2,3-butanediol (8.6 mg/100 ml). Blood concn of the parent compound and metabolites 18 hr after dosing with MEK were: MEK (6.2 mg/100 ml); 2-butanol (0.6 mg/100 ml); 3-hydroxy-2-**butanone** (1.4 mg/100 ml); and 2,3-butanediol (25.6 mg/100 ml).
[Dietz FKJ, Traiger GJ; Toxicology 14: 209-14 (1979)]**PEER REVIEWED**

MEK has been reported to be a metabolic end product of natural gas (methane 88%, ethane 5%, propane 5%, iso-butane 2%, with traces of t-butyl mercaptan and methyl acrylate) inhaled for 2 hr by ICR mice ... In an in vivo study of the metabolism of propane, n-butane and iso-butane inhaled for 1 hr by ICR mice, it was found that n-butane gave rise to sec-butanol and MEK ... In vitro studies showed that mouse liver microsomal preparations metabolized n-butane to sec-butanol, the precursor of MEK ... Inhalation by

male Sprague-Dawley rats of sec-butanol at concn of 5900 mg/cu m (2000 ppm) for 3 days or 1475 mg/cu m (500 ppm) for 5 days caused marked enzyme induction of cytochrome P-450 in liver and kidney but other butanol isomers did not have this effect ... The authors concluded that the mechanism of induction was via the sec-butanol metabolite MEK.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.51 (1993)]**PEER REVIEWED**

... the toxic effects of MEK and 2-butanol were essentially identical in rats, and that 2-butanol was rapidly oxidized to MEK. ... identified the metabolites of MEK in guinea pigs as 2-butanol, 3-hydroxy-2-**butanone** and 2,3-butanediol. They hypothesized that the metabolism followed both oxidative and reductive pathways, with the latter leading to the production of 2-butanol.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.52 (1993)]**PEER REVIEWED**

In rats exposed by inhalation to 1760 mg MEK/cu m (600 ppm), there were only marginal effects on microsomal cytochrome P-450 activities ... However, a daily dose of 1.4 mL MEK per kg for 3 days incr the amounts of ethanol- and phenobarbital-inducible cytochromes P-450 ...
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.53 (1993)]**PEER REVIEWED**

In a study on male Sprague-Dawley rats, pretreatment with MEK elevated total microsomal cytochrome P-450 and NADPH-dependent cytochrome-c-reductase, the rates of oxidation of N-nitrosodimethylamine, benzphetamine and pentoxyresorufin, and also the levels of immunoreactive protein for both P-450 isozymes ... In a study of hepatotoxicity in rats, ... found that MEK incr liver cytochrome P-450 content (33-86%) and glutathione-S-transferase (GST) activity (42-64%) but had no effect on serum glutamate dehydrogenase (GLDH) activity. ... studied the effects on hepatic cytochrome P-450 activities of repeated daily doses of 1.87 mL/kg given by gavage to male Fischer-344 rats. The activity of 7-ethoxy coumarin-O-deethylase was incr by up to 500% after 1 to 7 days of MEK treatment, but there was practically no change in benzphetamine-N-demethylase activity. In another study in male Sprague-Dawley rats, admin of MEK by gavage cause an incr in hepatic acetanilide hydroxylase and a marginal incr in aminopyrine-N-demethylase activities ... .
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.53 (1993)]**PEER REVIEWED**

MEK has been identified as a minor but normal constituent of urine ... serum and urine of diabetics ... and expired air ... . Its production in the body has been attributed to isoleucine catabolism ... studies ... indicate that the same metabolites are produced and excreted in humans as in experimental animals. ... further indicated that in an inhalation exposure to 590 mg MEK/cu m (200 ppm) the calculated areas under the curves of blood solvent concn versus time (AUC) for MEK and 2,3-butanediol were equal, which suggests that MEK is almost completely transformed to 2,3-butanediol. The bulk of MEK absorbed thus enters the general metabolism and is transformed to simple compounds like carbon dioxide and water.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.55 (1993)]**PEER REVIEWED**

METHYL ETHYL KETONE

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Absorption, Distribution & Excretion:

Measurable (2.54 to 13 ug/l) quantities of **methyl ethyl ketone** appeared in expired air of adult humans 3 min following dermal exposure to 100 ml **methyl ethyl ketone** applied to 91.5 sq cm of skin.
[Wurster; J Pharm Sci 54: 554 (1965)]**PEER REVIEWED**

Ketones are readily absorbed through the intact skin. Usually they are rapidly excreted ... in the expired air. /Ketones/
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 1170]**PEER REVIEWED**

Workers occupationally exposed to **methyl ethyl ketone (**MEK) were examined. ... Workers exposed to 300 micrograms per liter MEK, the aveolar concn was 30% of the environmental concn. Lung uptake averaged 1.05 mg/min. The blood concn of MEK ranged from 842 to 9573 ug/l, with a mean of 2630 ug/l. Blood concn of MEK were strongly correlated with alveolar concn. MEK was more soluble in heart and muscle tissue than in lung tissue or fat. Urinary MEK excretion ranged from 120 to 1120 mg/l, with a mean of 487 mg/l. ... MEK was not persistent in the tissues. ... Urinary excretion of MEK and acetylmethylcarbinol are only around 0.1% of MEK lung absorption, the main pathway through which MEK is eliminated is unknown.
[Perbellini L et al; Intern Arch Occup Environ Health 54 (1): 73-81 (1984)]**PEER REVIEWED**

ALTHOUGH ABSORPTION ... THROUGH THE SKIN MAY OCCUR, IT HAS BEEN SHOWN THAT IT IS LOW IN TOXICITY BY THIS ROUTE.
[Patty, F. (ed.). Industrial Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New York: Interscience Publishers, 1963. 1732]**PEER REVIEWED**

Percutaneous absorption of MEK appears to be rapid ... MEK was present in the exhaled air of human subjects within 2.5-3.0 min after it was applied to normal skin of the forearm, and the concn of MEK in exhaled air reached a plateau in 2-3 hr. The rate of absorption was controlled mainly by the moisture content of the skin. With dry skin, absorption was slow, and it took 4-5 hr for the concn of MEK in expired air to attain a plateau. With moist skin, absorption was very rapid initially. MEK was detected in expired air in measurable concn within 30 sec after an application of MEK to the forearm, and a max concn in expired air, averaging 4X the plateau level for normal and dry skin, was achieved in 10-15 min.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.49 (1993)]**PEER REVIEWED**

The absorption of MEK via the lungs was examined ... in a study of workers exposed in industrial workplace. The MEK concn in alveolar and expired air correlated significantly with the environmental concn, and averaged 30% of the latter. In more recent studies ... values for pulmonary absorption ranging from 41.1% to 55.8% were obtained. ... Deeper inhalation incr the alveolar volume relative to the dead space (the non-alveolar volume of the respiratory system), and thus incr the apparent absorption ... .

[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.49 (1993)]**PEER REVIEWED**

Results of studies ... indicated a rapid transfer of MEK vapor into the blood stream. ... the concn of MEK in the blood and urine were significantly correlated with the environmental concn, indicating rapid transfer to the blood and thence to other tissues. In human volunteer subjects, exercise during exposure markedly incr the MEK level in blood in comparison with sedentary behavior ... indicating that the blood MEK level also depended on the rate of uptake. ... also found significant correlations between environmental levels of MEK and amounts excreted in the urine of exposed workers. The concn of MEK in urine rose from essentially 0 to 70% of its max value during the first 2 hr of an 8-hr shift ... .
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.50 (1993)]**PEER REVIEWED**

... studied biological monitoring of occupational exposure to MEK in 67 healthy male workers employed in plastic bag or video-tape production. Their ages ranged between 18 and 52 yr with an average working experience of 8.6 yr. for the majority of the workers, atmospheric MEK concn were in the range of 30-885 mg/cu m (10-300 ppm). MEK concn in urine, blood and exhaled air were measured once/week at the end of a shift. About 10% of absorbed MEK was eliminated in the exhaled air. Following exposure to 590 mg/cu m (200 ppm), the urinary concn was 5.1 umol/L or 4.11 mg/g creatinine. The correlation coefficients between atmospheric MEK concn and end-of-shift urine, blood and exhaled air were 0.89, 0.85, and 0.79, respectively. The authors also reported good correlation between blood and urinary MEK ... and between blood and exhaled air concn ... but poor correlation between exhaled air and urinary MEK concn.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.50 (1993)]**PEER REVIEWED**

In male rats given a large MEK dose (1505 or 1690 mg/kg) in water, blood concn reached maxima of 0.95 and 0.94 mg/mL 4 hr after ingestion and subsequently declined sharply, indicating protracted absorption of this dose from the GI tract ... .
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.51 (1993)]**PEER REVIEWED**

... intraperitoneal injection of MEK in research on metabolism and toxicity, suggest that absorption from the peritoneal cavity is rapid.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.51 (1993)]**PEER REVIEWED**

The distribution of MEK in human tissues was examined ... in two solvent-exposed workers who died suddenly of heart attacks at the workplace. The results of this study ... indicate that the solubility of MEK is similar for all tissues. ... With a blood/air partition coefficient of 202, MEK can reach equilibrium concn in a compartment in about 3 min. Distribution volumes were 6.0 for vessel-rich tissues, 39.6 for muscle and 12.8 for fat. Biological half-lives for the same tissues were 0.8, 21.8 and 23.3 min, respectively.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.51 (1993)]**PEER REVIEWED**

The results of in vitro measurements at 37 deg C of human tissue-gas partition coefficients, obtained by exposing samples of blood and tissue to a known concn of MEK ... The partition coefficients ranged

from 96 to 162, but did not exceed 111, with the exception of whole blood (125), blood plasma (133) and fat (162). Other blood-gas partition coefficients measurements for MEK are 202 ... and 215 ... .
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.51 (1993)]**PEER REVIEWED**

... provided evidence that MEK can enter the liver of rats and guinea-pigs, and ... reported that it can cross the placenta and enter the human fetus.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.51 (1993)]**PEER REVIEWED**

MEK and its metabolites are excreted by the lungs and kidneys. ... only 3% of the calculated absorbed dose during a 4-hr exposure to 590 mg MEK/cu m (200 ppm) was secreted unchanged in the exhaled air of volunteers after the exposure. The fractional elimination of unchanged substance however depends on the efficiency of metabolic clearance. Since metabolic saturation for MEK in humans begins at relatively low levels (about 100 ppm) of exposure ... proportionally greater amounts of MEK would be expected to be excreted via the lungs (and kidneys) at high exposure levels.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.55 (1993)]**PEER REVIEWED**

Relatively little of absorbed MEK is excreted unchanged via the kidneys; a study of occupationally exposed workers revealed that it is less than 0.1% of the alveolar uptake ... In a similar study of workers occupationally exposed to a mixture of solvents, the excretion of MEK and a major recognizable metabolite, 3-hydroxy-2-**butanone**, was 0.1% of alveolar uptake ... The concentrations of both MEK and 3-hydroxy-2-**butanone** in urine were significantly correlated with the environmental level of MEK. Other metabolites of MEK, 2-butanol or 2,3-butanediol ... identified in the serum of guinea pigs, were not detected in the urine of the exposed workers. ... however ... human excretion of 2,3-butanediol was individually variable but averaged 2% of the absorbed MEK. The urinary excretion of 2-butanol, a minor metabolite of MEK was examined ... clearance of 2-butanol admin by gavage in rabbits was about 14% of the admin dose and in the form of a glucuronide.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.55 (1993)]**PEER REVIEWED**

Absorption of methylethylketone is rapid via inhalation and ingestion, and the compound is presumably a moderate skin penetrant as well. Since methylethylketone is both water and lipid soluble, it is rather evenly distributed in tissues.
[Zenz, C., O.B. Dickerson, E.P. Horvath. Occupational Medicine. 3rd ed. St. Louis, MO., 1994 149]**PEER REVIEWED**

METHYL ETHYL KETONE

CASRN: 78-93-3

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[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.56

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[Schmidt R et al; Respiration 46 (4): 362-9 (1984)]**PEER REVIEWED**

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IT DOES NOT APPEAR TO BE NEUROTOXIC BY ITSELF, IT POTENTIATES NEUROTOXICITY OF OTHER HEXACARBONS; REPORTED IN HUMANS EXPOSED TO **METHYL ETHYL KETONE (**MEK) & N-HEXANE.
[ALTENKIRCH ET AL; J NEUROL 214: 152 (1977)]**PEER REVIEWED**

Methyl ethyl ketone potentiates carbon tetrachloride hepatoxicity in rats. Oral dosing with **methyl ethyl ketone** at 1.87, 2.4, or 1.2 ml/kg followed by ip injection with carbon tetrachloride at 0.1 ml/kg significantly enhanced the hepatotoxicity of carbon tetrachloride as measured by increased serum glutamic pyruvic transaminase activity and hepatic triglyceride concentration and decreased hepatic glucose-6-phosphatase activity.
[Traiger GJ, Bruckner JV; J Pharmacol Exp Ther 196: 493 (1976)]**PEER REVIEWED**

A study of the potential relationship between **methyl ethyl ketone** and 2,5-hexanedione was conducted. Male F344 rats weighing between 200 and 320 g were used. A sensorimotor/behavioral battery consisting of two simple reflex tests, hind limb grasp and hind limb place, and two complex function tests, balance beam and accelerating rotorod performance, was used for identification and quantification of neurological deficits. ... The enhancement of 2,5-hexanedione induced toxicity by **methyl ethyl ketone** could be correlated with higher tissue exposures of 2,5-hexanedione in animals receiving the combined treatment. ... **Methyl ethyl ketone** may compete with 2,5-hexanedione for critical and non-critical binding sites at the target neurofilament proteins.
[Ralston WH et al; Toxicol Appl Pharm 81 (2): 319-27 (1985)]**PEER REVIEWED**

The effects of acute exposure to toluene and **methyl ethyl ketone (**MEK) singly and in combination were investigated. ... The effects of these chemicals on behavior and body burden were determined. ... MEK had no effect on any measures. Behavior performance was not affected by the combination of toluene and MEK. Body burden of the two solvents was not additive. ... Neither chemical potentiated the effect of the other at the concentrations studied.
[Dick RB et al; Int Arch Occup Environ Health 54 (2): 91-109 (1984)]**PEER REVIEWED**

... An important observation was the marked potentiation of peripheral neurotoxicity observed when animals were exposed to n-butyl ketone in combination with **methyl ethyl ketone** at a ratio of 1:5, n-butyl ketone: **methyl ethyl ketone.** The latter solvent showed no neurotoxic effect alone.
[Saida K et al; J Neuropathol Exp Neurol 35 (3): 207-25 (1976)]**PEER REVIEWED**

... The toxic neuropathy induced by **methyl ethyl ketone** is clinically and morphologically identical with that induced by n-hexane and methyl butyl ketone. **Methyl ethyl ketone** can act synergistically with n-hexane to produce toxic neuropathy.
[Alterkirch H et al; J Neurology 214: 137-52 (1977)]**PEER REVIEWED**

Ingestion of ethanol (0.8 g/kg) combined with an inhalation exposure to MEK (590 mg/cu m, 200 ppm) inhibited the oxidative metabolism of MEK and led to a marked incr in the blood concn of MEK ... There was a concurrent, even more pronounced elevation of the blood 2-butanol concn; the most likely explanation is competitive inhibition by ethanol of the oxidation of 2-butanol back to MEK. Ethanol also appeared to interact with the further biotransformation of 2,3-butanediol as the urinary excretion of the metabolite was incr. Co-exposure with xylene, however, had no effect on the human metabolism or rate of elimination of MEK ... .
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.57 (1993)]**PEER REVIEWED**

... found that MEK and certain other polar aprotic solvents were strong inducers of aneuploidy in the yeast. The induction of aneuploidy by MEK was markedly potentiated by coexposure to ethyl acetate ... or with nocodazol ... .
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.80 (1993)]**PEER REVIEWED**

MEK interacts with hexacarbon compounds and potentiates their neurotoxicity ... Potentially MEK co-exposure could affect the metabolism of the hexacarbon compounds or the toxic process by which the hexacarbons induce the neuropathy. ... The metabolic pathway involves hepatic microsomal oxidation to 2,5-hexanedione, the proximate neurotoxicant, which is thought to induce cross-linking of neurofilaments, blockage of transport at the node of Ranvier, and swelling from accumulated neurofilaments proximal to the nodes and axonal degeneration distal to the nodes.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.101 (1993)]**PEER REVIEWED**

Carbon tetrachloride (CCl_4), chloroform ($CHCl_3$) and related haloalkane solvents are liver and kidney poisons as well as central nervous depressants ... It has long been known that the hepatotoxic action of CCl_4 is potentiated by ethanol, and more recently that the hepatic and/or renal toxicity of CCl_4, $CHCl_3$, trichloroethylene, 1,1,2-trichloroethane and related compounds is potentiated by n-hexane, ethanol, isopropanol, acetone, MEK, MBK, 2,5-HD, and other ketones or chemicals that are metabolized to ketones ... Even an incr of naturally occurring ketones in the body via diabetes can precipitate potentiation. Decr the transformation of isopropanol to acetone by the admin of an inhibitor of alcohol dehydrogenase, pyrazole, has reduced potentiation of haloalkane toxicity. Although the phenomenon is referred to as haloalkane toxicity, experimental work in general appears largely or entirely limited to chlorinated compounds, and specific studies on MEK are limited to interactions with CCl_4 and $CHCl_3$.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.115 (1993)]**PEER REVIEWED**

METHYL ETHYL KETONE

CASRN: 78-93-3

For other data, click on the Table of Contents

Pharmacology:

Interactions:

IT DOES NOT APPEAR TO BE NEUROTOXIC BY ITSELF, IT POTENTIATES NEUROTOXICITY OF OTHER HEXACARBONS; REPORTED IN HUMANS EXPOSED TO **METHYL ETHYL KETONE (**MEK) & N-HEXANE.
[ALTENKIRCH ET AL; J NEUROL 214: 152 (1977)]**PEER REVIEWED**

Methyl ethyl ketone potentiates carbon tetrachloride hepatoxicity in rats. Oral dosing with **methyl ethyl ketone** at 1.87, 2.4, or 1.2 ml/kg followed by ip injection with carbon tetrachloride at 0.1 ml/kg significantly enhanced the hepatotoxicity of carbon tetrachloride as measured by increased serum glutamic pyruvic transaminase activity and hepatic triglyceride concentration and decreased hepatic glucose-6-phosphatase activity.
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[Ralston WH et al; Toxicol Appl Pharm 81 (2): 319-27 (1985)]**PEER REVIEWED**

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[Dick RB et al; Int Arch Occup Environ Health 54 (2): 91-109 (1984)]**PEER REVIEWED**

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[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.57 (1993)]**PEER REVIEWED**

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[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.101 (1993)]**PEER REVIEWED**

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[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.115 (1993)]**PEER REVIEWED**

METHYL ETHYL KETONE

CASRN: 78-93-3

For other data, click on the Table of Contents

Environmental Fate & Exposure:

Environmental Fate/Exposure Summary:

Methyl ethyl ketone's production and use as a solvent for coatings, resins, rubbers, plastics, pharmaceuticals, adhesives and rubber cements will result in its release to the environment through various waste streams. Its use as a starting material or intermediate in the manufacture of chemical products will also lead to its release to the environment. **Methyl ethyl ketone** occurs naturally as a metabolic byproduct of plants and animals and is released into the atmosphere by volcanoes and forest fires. Based on an experimental vapor pressure of 91 mm Hg at 25 deg C, **methyl ethyl ketone** is expected to exist solely as a vapor in the ambient atmosphere. Vapor-phase **methyl ethyl ketone** is degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals with an estimated atmospheric half-life of about 14 days. This compound is also expected to undergo photolysis in the atmosphere by natural sunlight. Photochemical degradation of **methyl ethyl ketone** by natural sunlight is expected to occur at approximately 1/5 the rate of degradation by photochemically produced hydroxy radicals. **Methyl ethyl ketone** is expected to have very high mobility in soils based upon measured Koc values of 29 and 34 obtained in silt loams. Volatilization from dry soil surfaces is expected based upon the vapor pressure of this compound. Volatilization from moist soil surfaces is also expected based upon the measured Henry's Law constant of 4.7X10-5 atm-cu m/mol. The volatilization half-life of **methyl ethyl ketone** from silt and sandy loams was measured as 4.9 days. This compound is expected to biodegrade under aerobic and anaerobic conditions. In water, **methyl ethyl ketone** is not expected to adsorb to suspended solids or sediment based upon its measured Koc values. Volatilization from water surfaces is expected to be an important environmental fate process given its Henry's Law constant. Estimated half-lives for a model river and model lake are 19 and 197 hours, respectively. Bioconcentration in aquatic organisms is considered low based upon an estimated BCF value of 1. Occupational exposure may be through inhalation and dermal contact with this compound at workplaces where **methyl ethyl ketone** is produced or used. The general population may be exposed to **methyl ethyl ketone** through the use of commercially available products containing this compound such as paints, adhesives, and rubber cements. Exposure will also arise from inhalation of ambient air and ingestion of drinking water and food that contains **methyl ethyl ketone. (**SRC)
PEER REVIEWED

Probable Routes of Human Exposure:

NIOSH has est worker exposure to **methyl ethyl ketone** at 3,031,000 ...
[Sittig, M. Handbook of Toxic and Hazardous Chemicals and Carcinogens, 1985. 2nd ed. Park Ridge, NJ: Noyes Data Corporation, 1985. 601]**PEER REVIEWED**

Artificial leather workers /are at risk of exposure/.
[Arena, J.M. and Drew, R.H. (eds.) Poisoning-Toxicology, Symptoms, Treatments. 5th ed. Springfield, IL: Charles C. Thomas Publisher, 1986. 358]**PEER REVIEWED**

NIOSH (NOES Survey 1981-1983) has statistically estimated that 1,221,857 workers (201,308 of these are female) are potentially exposed to **methyl ethyl ketone** in the US(1). Occupational exposure may be through inhalation and dermal contact with this compound at workplaces where **methyl ethyl ketone** is produced or used(SRC). The 8 hour TWA exposure to **methyl ethyl ketone** was 45.4 ppm in a survey of 50 occupationally exposed male subjects working in a magnetic videotape producing factory(2). These workers had average concns of **methyl ethyl ketone** of 2 ppm and 1.4 mg/l in breath and blood samples respectively(2). The mean concn of **methyl ethyl ketone** in the breathing zones of 47 US plants using polyurethane coatings was 4.33 ppm(3). **Methyl ethyl ketone** was detected in the breathing zones in 20 of 70 samples (mean concn 12 mg/cu m) obtained from autobody shops and spray paint shops in Australia(4).
[(1) NIOSH; National Occupational Exposure Survey (NOES) (1983) (2) Sia Gl et al; Environ Monit Assess 19: 401-11 (1991) (3) Myer HE et al; Am Ind Hyg Assoc J 54: 663-70 (1993) (4) Winder C, Turner PJ; Ann Occup Hyg 36: 385-94 (1992)]**PEER REVIEWED**

The general population may be exposed to **methyl ethyl ketone** through the use of commercially available products containing this compound such as paints, adhesives, and rubber cements(SRC). Exposure will also arise from inhalation of ambient air, ingestion of drinking water and food that contains **methyl ethyl ketone(**SRC). The average blood concn of **methyl ethyl ketone** in 600 non-occupationally exposed individuals in the US was 7.1 ppb(1).
[(1) Ashley DL et al; Clin Chem 40: 1401-04 (1994)]**PEER REVIEWED**

Body Burden:

Detected in 5 of 8 samples of mother's milk from 4 USA urban areas.
[(1) Pellizzari ED et al; Bull Environ Contam Toxicol 28: 322-8 (1982)]**PEER REVIEWED**

The kinetics of inhaled **methyl ethyl ketone (**MEK) in human volunteers was studied in an exposure chamber. Relative pulmonary uptake was about 53% throughout a 4 hr exposure period at 200 ppm. Blood MEK concentration rose steadily until the end of exposure. Repeated bicycle exercise increased the overall blood MEK level markedly in comparison to sedentary activity, with transient peaks in association with cycling; thus blood MEK concentration depended both on the rate of uptake and the amount taken up. Only 3% of the absorbed dose was excreted unchanged by exhalation. A well known metabolite of MEK, 2,3-butanediol, was detected in the urine with maximum rates of excretion at about 6 to 12 hr from the beginning of exposure. About 2% of the MEK dose taken up by the lungs was excreted in the urine as 2,3-butanediol. ... Elimination of MEK in blood appeared to exhibit two phases: the initial alpha-phase (T1/2= 30 min; kel alpha= 0.023) over the first post-exposure hour, followed by the terminal beta-phase (T1/2= 81 min; kel beta= 0.009).
[Liira J et al; Int Arch Occup Environ Health 60 (3): 195-200 (1988)]**PEER REVIEWED**

Worker exposures were investigated in April 1983 at the Hoover Company, North Canton, Ohio. ... Area and personal air samples for numerous contaminants were collected and nonionizing radiation levels were measured. ... General medical questionnaires and blood tests for **methyl ethyl ketone (**MEK) were given to exposed workers. ... No respiratory symptoms or pulmonary function disorders were identified in the foundry workers, and MEK was detected in the blood of only one worker at 1.4 ug/ml. ...

[NIOSH; Health Hazard Evaluation Report No. HETA-82-280-1407 (1984)]**PEER REVIEWED**

Natural Pollution Sources:

Methyl ethyl ketone occurs naturally as a metabolic byproduct of plants and animals and is released into the atmosphere by volcanoes and forest fires(1).
[(1) Graedel TE et al; Atmospheric Chemical Compounds. NY,NY: Academic Press p. 263 (1986)]**PEER REVIEWED**

Artificial Pollution Sources:

Methyl ethyl ketone's production and use as a solvent for coatings, resins, rubbers, plastics, pharmaceuticals, adhesives and rubber cements(1-3) will result in its release to the environment through various waste streams(SRC). Its use as a starting material or intermediate in the manufacture of chemical products(2,3) will also lead to its release to the environment(SRC).
[(1) Budvari S; Merck Index, 12th ed, Whitehouse Station,NJ: Merck & Co. p. 1773 (1996) (2) Browning E; Toxicity and Metabolism of Industrial Solvents. NY,NY: American Elsevier (1965) (3) Lewis RJ Sr ed; Hawley's Condensed Chemical Dictionary. 12th ed NY,NY: Van Nostrand Rheinhold Co p. 768 (1993)]**PEER REVIEWED**

Water pollution: Polyvinyl chloride pipe cement used for joint connection caused 4.5 ppm, 6 months after polyvinyl chloride pipe installation and 2.2 ppm after 8 months (at equilibrium condition-reached in about 48 hr).
[Verschueren, K. Handbook of Environmental Data of Organic Chemicals. 2nd ed. New York, NY: Van Nostrand Reinhold Co., 1983. 851]**PEER REVIEWED**

Environmental Fate:

TERRESTRIAL FATE: Measured Koc values of 29 and 34 were obtained for **methyl ethyl ketone** in silt loams(1). Based on a recommended classification scheme(2), **methyl ethyl ketone** is expected to have very high mobility in soil(SRC). Volatilization of **methyl ethyl ketone** from dry soil surfaces is expected based upon an experimental vapor pressure of 91 mm Hg at 25 deg C(3). Volatilization from moist soil surfaces(SRC) is also expected given the measured Henry's Law constant of 4.7X10-5 atm-cu m/mole(4). The volatilization half-life of **methyl ethyl ketone** from silt and sandy loams was measured as 4.9 days(5). **Methyl ethyl ketone** is expected to biodegrade under both aerobic and anaerobic conditions as indicated by numerous screening tests(6-9).
[(1) Walton BT et al; J Environ Qual 21: 552-58 (1992) (2) Swann RL et al; Res Rev 85: 23 (1983) (3) Alarie Y et al; Toxicol Appl Pharmacol 134: 92-99 (1995) (4) Bhattacharaya SK et al; Water Res 30: 3099-3105 (1996) (5) Anderson TA et al; J Environ Qual 20: 420-24 (1991) (6) Bridie Al, et al; Water Res 13: 627-30 (1979) (7) Price KS et al; J Water Pollut Control Fed 46: 63-77 (1974) (8) Bhattacharaya SK et al; Wat Res 30: 3099-3105 (1996) (9) Suflita JM, Mormile MR; Environ Sci Technol 27: 976-78 (1993)]**PEER REVIEWED**

AQUATIC FATE: Based on experimental Koc values of 29 and 34 obtained in silt loams(1), and a

recommended classification scheme(2), **methyl ethyl ketone** is not expected to adsorb to suspended solids and sediment in water(SRC). **Methyl ethyl ketone** is expected to volatilize from water surfaces(3,SRC) based on the measured Henry's Law constant of 4.7X10-5 atm-cu m/mole(4). Estimated half-lives for a model river and model lake are 19 and 197, hours respectively(3,SRC). Biodegradation of this compound is expected based upon numerous screening tests(5-8). According to a classification scheme(9), an estimated BCF value of 1(3,SRC), from an experimental log Kow of 0.29(10,SRC), suggests that bioconcentration in aquatic organisms is low(SRC).
[(1) Walton BT et al; J Environ Qual 21: 552-58 (1992) (2) Swann RL et al; Res Rev 85: 23 (1983) (3) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington DC: Amer Chem Soc pp. 4-9 (1990) (4) Bhattacharaya SK et al; Water Res 30: 3099-3105 (1996) (5) Bridie Al, et al; Water Res 13: 627-30 (1979) (6) Price KS et al; J Water Pollut Control Fed 46: 63-77 (1974) (7) Bhattacharaya SK et al; Wat Res 30: 3099-3105 (1996) (8) Suflita JM, Mormile MR; Environ Sci Technol 27: 976-78 (1993) (9) Franke C et al; Chemosphere 29: 1501-14 (1994) (10) Hansch C et al; Exploring QSAR Hydrophobic, Electronic and Stearic Constants Washington,DC: Amer Chem Soc (1995)]**PEER REVIEWED**

ATMOSPHERIC FATE: According to a model of gas/particle partitioning of semivolatile organic compounds in the atmosphere(1), **methyl ethyl ketone,** which has an experimental vapor pressure of 91 mm Hg at 25 deg C(2), will exist solely as a vapor in the ambient atmosphere. Vapor-phase **methyl ethyl ketone** is degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals(SRC); the half-life for this reaction in air is estimated to be about 14(3,SRC) days. **Methyl ethyl ketone** is also expected to undergo photodecomposition in the atmosphere by natural sunlight(4,5). Photochemical degradation of **methyl ethyl ketone** by natural sunlight is expected to occur at approximately 1/5 the rate of degradation by photochemically produced hydroxyl radicals(5).
[(1) Bidleman TF; Environ Sci Technol 22: 361-367 (1988) (2) Alarie Y et al; Toxicol Appl Pharmacol 134: 92-99 (1995) (3) Atkinson R; J Phys Chem Ref Data (1989) (4) Raber W et al; pp. 364-70 in Phys Chem Behav Atmos Pollut 5th ed Restelli G, Angeletti G eds, Kluwer: Dordecht, Netherlands (1990) (5) Altshuller AP; J Atmos Chem 13: 155-82 (1991)]**PEER REVIEWED**

Environmental Biodegradation:

Methyl ethyl ketone (MEK) is readily oxidized by microorganisms in activated sludge following selection and/or adaptation, with over 80% being removed in 24 hr. Metabolism in unacclimated sludges is slow.
[USEPA; Methyl Ethyl Ketone III: Exposure Aspects USEPA Contract No. 68-01-6147 (1981)]**PEER REVIEWED**

Biological oxygen demand (BOD) after 5 days @ 20 deg C: 1.515-1.92; 2.24 (std dilution technique, normal sewage seed); 5.3 (Dutch std test method); 1.81 (@ 10 mg/l, unadapted sewage, 1 days lag period).
[Verschueren, K. Handbook of Environmental Data of Organic Chemicals. 2nd ed. New York, NY: Van Nostrand Reinhold Co., 1983. 851]**PEER

REVIEWED**

Chemical oxygen demand (COD): 2.20-2.31; 5.3 (Dutch std test method); theoretical oxygen demand (ThOD): 2.44; permanganate test value: 0.29.
[Verschueren, K. Handbook of Environmental Data of Organic Chemicals. 2nd ed. New York, NY: Van Nostrand Reinhold Co., 1983. 851]**PEER REVIEWED**

Using standard BOD and COD dilution techniques and a sewage inoculum, a theoretical BOD of 83% and a theoretical COD of 95% was reported over a 5 day incubation period(1). The percent theoretical BOD of **methyl ethyl ketone** in freshwater was reported as 76%, 82%, 84% and 89% over 5, 10 15 and 20 day incubation periods respectively(2). The percent theoretical BOD of **methyl ethyl ketone** in synthetic saltwater was reported as 32%, 62%, 63% and 69% over 5, 10 15 and 20 day incubation periods respectively(2). 92-95% biodegradation was reported when 0.25 mg/l of **methyl ethyl ketone** was fed through an activated sludge from a wastewater treatment plant over a 3 week incubation period(3). The percent theoretical methane recovery of **methyl ethyl ketone** in an anaerobic aquifer was 89% over a 3 week incubation period following a 15 day acclimation period(4).
[(1) Bridie Al, et al; Water Res 13: 627-30 (1979) (2) Price KS et al; J Water Pollut Control Fed 46: 63-77 (1974) (3) Bhattacharaya SK et al; Wat Res 30: 3099-3105 (1996) (4) Suflita JM, Mormile MR; Environ Sci Technol 27: 976-78 (1993)]**PEER REVIEWED**

Environmental Abiotic Degradation:

The rate constant for the vapor-phase reaction of **methyl ethyl ketone** with photochemically-produced hydroxyl radicals has been measured as 1.15X10-12 cu cm/molecule-sec at 25 deg C(1). This corresponds to an atmospheric half-life of about 14 days at an atmospheric concn of 5.0X10+5 hydroxyl radicals per cu cm(1,SRC). **Methyl ethyl ketone** is also expected to undergo photodecomposition in the atmosphere by natural sunlight(2,3). Based on the actinic fluxes within the planet boundary layer, along with an estimated quantum yield and absorption cross section, the rate of photodissociation of **methyl ethyl ketone** by natural sunlight is approximately 1/5 the rate of dissociation by hydroxyl radicals(3). This compound is not expected to undergo hydrolysis in the environment due to a lack of functional groups which hydrolyze(SRC).
[(1) Atkinson R; J Phys Chem Ref Data (1989) (2) Raber W et al; pp. 364-70 in Phys Chem Behav Atmos Pollut 5th ed Restelli G, Angeletti G eds, Kluwer: Dordecht, Netherlands (1990) (3) Altshuller AP; J Atmos Chem 13: 155-82 (1991)]**PEER REVIEWED**

Environmental Bioconcentration:

An estimated BCF value of 1 was calculated for **methyl ethyl ketone(**SRC), using an experimental log Kow of 0.29(1) and a recommended regression-derived equation(2). According to a classification scheme(3), this BCF value suggests that bioconcentration in aquatic organisms is low(SRC).
[(1) Hansch C et al; Exploring QSAR Hydrophobic, Electronic and Stearic Constants Washington DC: Amer Chem Soc (1995) (2) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington DC: Amer Chem Soc pp. 5-4, 5-10 (1990) (3) Franke C et al; Chemosphere 29: 1501-14 (1994)]**PEER REVIEWED**

Soil Adsorption/Mobility:

Measured Koc values of 29 and 34 were obtained for **methyl ethyl ketone** in silt loams(1). Based on a recommended classification scheme(2), **methyl ethyl ketone** is expected to have very high mobility in soil(SRC).
[(1) Walton BT et al; J Environ Qual 21: 552-58 (1992) (2) Swann RL et al; Res Rev 85: 23 (1983)]**PEER REVIEWED**

Volatilization from Water/Soil:

The Henry's Law constant for **methyl ethyl ketone** was measured as 4.7X10-5 atm-cu m/mole(SRC) at 25 deg C(1). This value indicates that **methyl ethyl ketone** will volatilize from water surfaces(2,SRC). Based on this Henry's Law constant, the volatilization half-life from a model river (1 m deep, flowing 1 m/sec, wind velocity of 3 m/sec) is estimated as approximately 19 hours(2,SRC). The volatilization half-life from a model lake (1 m deep, flowing 0.05 m/sec, wind velocity of 0.5 m/sec) is estimated as approximately 197 hours(2,SRC). **Methyl ethyl ketone** is expected to volatilize from dry soil surfaces given its experimental vapor pressure of 91 mm Hg at 25 deg C(3,SRC). The volatilization half-life of **methyl ethyl ketone** from silt and sandy loams was measured as 4.9 days(4).
[(1) Bhattacharaya SK et al; Water Res 30: 3099-3105 (1996) (2) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington DC: Amer Chem Soc pp. 15-1 to 15-29 (1990) (3) Alarie Y et al; Toxicol Appl Pharmacol 134: 92-99 (1995) (4) Anderson TA et al; J Environ Qual 20: 420-24 (1991)]**PEER REVIEWED**

Environmental Water Concentrations:

DRINKING WATER: A Federal survey of public groundwater supplies detected **methyl ethyl ketone** in less than 5% of the samples(1). **Methyl ethyl ketone** was identified, not quantified, in drinking water supplies from 7 cities from varied sources and with different types of pollutant sources(2-4).
[(1) Dyksen JE, Hess AF III; J Amer Water Works Assoc 74: 394-403 (1982) (2) Coleman WE et al; pp. 305-207 in Analysis and Identification of Organic Substances in Water. Keith L ed Ann Arbor, MI Ann Arbor Press (1976) (3) Scheeman MA et al; Biomed Mass Spectrom 4: 209-11 (1974) (4) USEPA; New Orleans Area Water Supply Study. Draft Analytical Report by the Lower Mississippi River Facility, Slidell (1974)]**PEER REVIEWED**

GROUNDWATER: **Methyl ethyl ketone** was detected in groundwater at a coal strip-mine in Ohio at a concn of 650 mg/l(1). **Methyl ethyl ketone** was identified, not quantified, in on-site and off-site groundwater near a landfill in New Jersey(2). **Methyl ethyl ketone** was detected in the groundwater of a coal strip-mine in Lackawanne, PA at a maximum concn of 29,000 ppb(3). **Methyl ethyl ketone** was detected at an average concn of 12 ug/l in the groundwater of 19 solid waste disposal facilities in Wisconsin(4) and in the range of 0-91 ug/l in the groundwater of a landfill located in New Castle, DE(5). **Methyl ethyl ketone** was detected at an average concn of 60 ug/l in the groundwater of a chemical manufacturing facility in Alabama(6).
[(1) USEPA; Superfund Record of Decision : Summit National Site, Deerfield OH. USEPA/ROD/R85-88/068 (1988) (2) USEPA; Superfund Record

of Decision: Lipari Landfill Mantau Township, NJ. USEPA/ROD/RO2-88/074 (1988) (3) ATSDR; Health assessment for Beacon Heights Landfill National Priorities List (NPL) Site, Beacon Falls, Connecticut, Region 1. CERCLIS NO. CTD001145671. Agency for Toxic Substances and Disease Registry PB90-135971 (1990) (4) Battista JR, Connelly JP; VOC contamination at selected Wisconsin landfills - sampling results and policy implications. Wisc Dept of Natural Resources, Madison, WI. Publ-SW-094 (1989) (5) ATSDR; Health assessment for Tybouts Corner land (Tybouts) National Priorities List (NPL) site, Wilmington, New Castle County, Deleware, Region 3. CERCLIS NO. DED000606079. Agency for Toxic Substances and Disease Registry PB90-144387 (1989) (6) USEPA; Superfund Record of Decision: Ciba-Geigy (Mcintosh Plant), AL. USEPA/ROD/R04-89/056 (1989)]**PEER REVIEWED**

SURFACE WATER: **Methyl ethyl ketone** was identified, not quantified, in the Black River in Tuscaloosa, AL(1) and Newark Bay, NJ(2). **Methyl ethyl ketone** was detected in the Potomac River at a concn of less than 40 ug/l(3). **Methyl ethyl ketone** was detected in a creek in New Castle, DE near a landfill at concns of 0-11,000 ug/l(4).
[(1) Berstch W et al; J Chromatog 112: 701-18 (1975) (2) Gunster DG et al; Environ Pollut 82: 245-53 (1993) (3) Hall LWJR et al; Aquat Toxicol 10: 73-99 (1987) (4) ATSDR; Health assessment for Tybouts Corner land (Tybouts) National Priorities List (NPL) site, Wilmington, New Castle County, Deleware, Region 3. Agency for Toxic Substances and Disease Registry PB90-144387 (1989)]**PEER REVIEWED**

RAIN/SNOW: An unspecified concn of **methyl ethyl ketone** was detected in the rainfall in Japan(1). **Methyl ethyl ketone** was detected at concns of 0-0.47 ppb in the clouds in California and as trace amounts in fog-ice(2). **Methyl ethyl ketone** was detected in clouds (1,390 ng/l) and rainfall (139 ng/l) at a state park in North Carolina(3).
[(1) Kato T et al; Yokohama Kokuritsu Daigaku Kankyo Kagaku Kenkyu Senta Kiyo 6: 11-20 (1980) (2) Grosjean D, Wright B; Atmos Environ 17: 2093-6 (1983) (3) Aneja VP et al; J Air Waste Manage Assoc 43: 1239-44 (1993)]**PEER REVIEWED**

Effluent Concentrations:

Methyl ethyl ketone was detected in the leachate of several municipal landfills at concns between 110-6,600 ug/l(1). **Methyl ethyl ketone** was detected in the leachate of a sand and gravel pit near Utica, NY at a concn of 540 ug/l(2). **Methyl ethyl ketone** was detected in the leachate of an industrial landfill (53 mg/l) and a municipal landfill (0.11-27 mg/l)(3).
[(1) Christensen TH et al; Crit Rev Environ Sci Technol 24: 119-202 (1994) (2) USEPA; Superfund Record of Decision: Ludlow Sand and Gravel Site, Town of Paris Oneida County, NY USEPA/ROD/R02-88/067 (1988) (3) Brown KW, Donnelly KC; Haz Waste Haz Mater 5: 1-30 (1988)]**PEER REVIEWED**

Methyl ethyl ketone was detected in the effluent of a municipal landfill in Quebec, Ontario at concns of

5,200 ppb and 3092 ppb(1). **Methyl ethyl ketone** was identified, not quantified in the emissions of a waste incinerator in West Germany(2), automobiles(3) and common household waste(4-7). **Methyl ethyl ketone** was detected in the effluent from a solid waste composting plant at concns of 130 ug/cu m (background air), 25,500 ug/cu m(tipping area), 1,400 ug/cu m (shredder), 9,400 ug/cu m(indoor air), 36,000 ug/cu m (digester), 4,300 ug/cu m(fresh compost), 8,700 ug/cu m(middle age compost), 14,500 ug/cu m(old compost) and 1,400 ug/cu m(curing region)(8). **Methyl ethyl ketone** was identified, not quantified, in the emissions of 200 out of 1,026 common household products(9). **Methyl ethyl ketone** was detected in the emissions of a photocopying machine at rates of less than 100 ug/hr to 380 ug/hr(10). **Methyl ethyl ketone** was detected at a concn of 974 ug/cu m in the emissions of active compost at a composting facility in Virginia(11).
[(1) Brosseau, Heitz M; Atmos Environ 25A: 1473-77 (1994) (2) Jay K, Stieglitz L; Chemosphere 30: 1249-60 (1995) (3) Harley RA et al; Environ Sci Technol 26: 2395-2408 (1992) (4) Wilkins CK, Larsen K; J High Resol Chromatogr 18: 373-77 (1995) (5) Wilkins K, Larsen K; Chemosphere 31: 3225-36 (1995) (6) Wilkins K, Larsen K; Chemosphere 32: 2049-55 (1996) (7) Wilkins K; Chemosphere 29: 47-53 (1994) (8) Eitzer BD; Environ Sci Technol 29: 896-902 (1995) (9) Sack TM et al; Atmos Environ 26A: 1063-70 (1992)(10) Leovic KW et al; J Air Waste Manage Assoc 46: 821-29 (1996) (11) Vandurme GP et al; Water Environ Res 64: 19-27 (1992)]**PEER REVIEWED**

Sediment/Soil Concentrations:

Methyl ethyl ketone was detected in the soil of a coal strip mine in Ohio at mean concns of 1,682 ug/kg (surface soil), 11,750 ug/kg (2-4 feet), 38,000 ug/kg (4-6 feet), 5,368 ug/kg (6-8 feet)(1). **Methyl ethyl ketone** was identified, not quantified, in the subsurface soil of a gravel mine in Tennessee(2). **Methyl ethyl ketone** was detected at an average concn of 1,615 ug/kg in the soil of an unauthorized hazardous waste disposal facility in New Jersey(3). **Methyl ethyl ketone** was detected at an average concn of 32 ug/kg in the soil of a waste disposal facility in Kansas(4).
[(1) USEPA; Superfund Record of Decision: Summit National Site, Deerfield OH. USEPA/ROD/R85-88/068 (1988) (2) USEPA; Superfund Record of Decision: Galloway Ponds Site, Galloway, TN. USEPA/ROD/R04-86/013 (1987) (3) USEPA; Superfund Record of Decision: Lang Property Pemberton Township, NJ USEPA/ROD/R02-86/031 (1987) (4) USEPA; Superfund Record of Decision: Doepke Disposal (Holliday), KS USEPA/ROD/R07-89/032 (1989)]**PEER REVIEWED**

Atmospheric Concentrations:

The presence of solvents such as toluene, xylene, **methyl ethyl ketone,** and other similar products in the indoor air of an automobile body repair shop, an offset printing facility and the adjacent dwellings was monitored, and the individual exposure of the corresponding workers and residents was tested by biological monitoring of exhaled breath and by personal air sampling. The concentrations of solvents tested in the air of both sites surveyed were lower than prevailing Dutch Maximum Allowable Concentration levels. The levels of solvents recorded in the air of apartments situated on top of the facilities surveyed were significantly higher than the levels recorded in the surrounding dwellings. The levels of **methyl ethyl ketone,** toluene and xylene in personal air samples of employees at the body shop

were 1.5 times higher than in ambient air. The level of toluene in alveolar air of residents living above the automobile repair shop was 50 percent higher than that recorded in spot samples. The levels of other solvents were equal to or lower than the detection level. At the offset printing facility, toluene, xylene, butylacetate, 2-ethoxyethanol and cyclohexanone in air and in personal air samples followed the same general pattern identified for the body shop. In a dwelling next to the shop and in an apartment on top of the shop, the concentrations ranged from 3 to 9 percent and 14 to 19 percent, respectively, of the levels recorded inside the facility itself.
[Verhoeff AP et al; Int Arch Occup Environ Health 59 (2): 153-63 (1987)]**PEER REVIEWED**

URBAN/SUBURBAN: **Methyl ethyl ketone** was detected at a mean concn of 1.5 ppb in Boston, MA(1). **Methyl ethyl ketone** was detected at mean concns of 1.35 ppb in Boston, MA, and 5.1 ppb in Houston, TX(2). The average concn of **methyl ethyl ketone** at 25 urban locations in the US was 1.4 ug/cu m(3). **Methyl ethyl ketone** was detected at a mean concn of 1.67 ppb in Los Angeles, CA(4) and in the Caldecott Tunnel in San Francisco, CA at a concn of 1.67 mg/l(5). **Methyl ethyl ketone** was detected at average concns of 0.222-1.366 ppb in Grenoble, France(6). An average concn of 0.638 ppb of **methyl ethyl ketone** was obtained from 714 atmospheric samples in the US(7).
[(1) Reiss R et al; J Air Waste Manage Assoc 45: 811-22(1995) (2) Kelly TJ et al; Environ Sci Technol 27: 1146-53 (1993) (3) Kelly TJ et al; Ambient concn summaries for Clean Air Act. Title III. Hazardous Air Pollutants. USEPA Contract No 68-D80082 USEPA/600/R-94/090 (1993) (4) Grosjean E et al; Environ Sci Technol 30: 2687-2703 (1996) (5) Kirschstetter TW et al; Environ Sci Technol 30: 661-70 (1996) (6) Foster P et al; Pollut Atmos: 175-91 (1991) (7) Shah JJ, Heyerdahl EK; Environ Sci Technol 22: 1381-88 (1988)]**PEER REVIEWED**

RURAL/REMOTE: **Methyl ethyl ketone** was detected at an average concn of 2.40 ng/l in the air of a state park in North Carolina(1). **Methyl ethyl ketone** was detected at an average concn of 18 ug/cu m at rural locations in Canada(2) and concns of 1.8-3.3 ppb in a rural location in Louisiana(3).
[(1) Aneja VP et al; J Air Waste Manage Assoc 43: 1239-44 (1993) (2) Chan CC et al; J Air Waste Manage Assoc 40: 62-67 (1990) (3) Khalil MAK, Rasmussen RA; J Air Waste Manage Assoc 42: 810-13 (1992)]**PEER REVIEWED**

SOURCE AREAS: **Methyl ethyl ketone** was detected at a median concn of 64 parts per trillion and a range of 10-1,900 parts per trillion(1) in source dominated areas in New Jersey(1). **Methyl ethyl ketone** was detected at a concn of 94 ppm near a reclamation plant(2).
[(1) Brodzinsky R, Singh HB; Volatile Organic Chemicals in the Atmos SRI International Contract 68-02-3452 (1982) (2) Lande SS et al; Investigation of Selected Potential Environmental Contaminants: Ketonic Solvents 331 p USEPA 560/2-76-003 (1976)]**PEER REVIEWED**

INDOOR AIR: **Methyl ethyl ketone** was detected at an average concn of 17.8 ug/cu m at dwellings in Canada(1) and 2.4 ppb in buildings in Boston, MA(2). **Methyl ethyl ketone** was detected in 2 federal office buildings in Portland, OR at concns between 2.0 and 40.9 ug/cu m(3). Four indoor air samples in the US had average concns of MEK of 9.238 ppb(4).
[(1) Chan CC et al; J Air Waste Manage Assoc 40: 62-67 (1990) (2)

Reiss R et al; J Air Waste Manage Assoc 45: 811-22 (1995) (3) Hodgeson AT et al; J Air Waste Manage Assoc 41: 1461-68 (1991) (4) Shah JJ, Heyerdahl EK; Environ Sci Technol 22: 1381-88 (1988)]**PEER REVIEWED**

Food Survey Values:

NON-ALCOHOLIC BEVERAGES 70 PPM; ICE CREAM, ICES, ETC 270 PPM; CANDY 100 PPM; BAKED GOODS 100 PPM
[Fenaroli's Handbook of Flavor Ingredients. Volume 2. Edited, translated, and revised by T.E. Furia and N. Bellanca. 2nd ed. Cleveland: The Chemical Rubber Co., 1975. 59]**PEER REVIEWED**

Methyl ethyl ketone was detected in Swiss cheese (0.3 ppm) and cream (0.154-0.177 ppm)(1). **Methyl ethyl ketone** was identified, not quantified, in the volatiles of roasted barley, bread, honey, chicken, oranges, black tea, and rum(1), kiwi fruit(2), chickpea seeds(3), mutton, chicken and beef(4). **Methyl ethyl ketone** was detected at a concn of 1.83 ug/g in rotten mussels in Japan(5).
[(1) Lande SS et al; Investigation of Selected Potential Environmental Contaminants: Ketonic Solvents. 331 pp. USEPA 560/2-76-003 (1976) (2) Tatsuka K et al; J Food Sci 38: 2176-80 (1990) (3) Rembold H et al; J Agric Food Chem 37: 659-62 (1989) (4) Shahidi F et al; CRC Crit Rev Food Sci Nature 24: 141-243 (1986) (5) Yasuhara A; J Chromatogr 409: 251-58 (1987)]**PEER REVIEWED**

Plant Concentrations:

32 samples of southern pea seed, Vigna unguiculata, were analyzed for volatiles. **Methyl ethyl ketone (**MEK) was found in all samples and the mean concn was 151 + or - 80 ppb (74 to 390 ppb).
[Fisher GS et al; J Agric Food Chem 27: 7-11 (1979)]**PEER REVIEWED**

Methyl ethyl ketone is emitted from pencil cedar, Zeravshan juniper, European firs and Evergreen cyprus(1). **Methyl ethyl ketone** was detected in 32 of 32 samples of southern pea seeds at a mean concn of 151 ppb(2).
[(1) Singh HB, Zimmerman PB; Adv Environ Sci Technol 24: 177-235 (1992) (2) Fisher GS et al; J Agric Food Chem 27: 7-11 (1979)]**PEER REVIEWED**

Milk Concentrations:

Milk 0.077-0.079 ppm, milk fat 8 ppm(1).
[(1) Lande SS et al; Investigation of Selected Potential Environmental Contaminants: Ketonic Solvents p. 102 USEPA 560/2-76-003 (1976)]**PEER REVIEWED**

Methyl ethyl ketone was identified, not quantified in human milk samples in Bayonne, NJ(1) Pittsburgh, PA(1) Baton Rouge, LA(1) and Australia(2). **Methyl ethyl ketone** was identified, not quantified in 5 of 8 samples of human milk from 4 US urban areas(3).
[(1) Erickson MD et al; Acquisition and chemical analysis of mother's milk for selected toxic substances. USEPA-560/13-80-029. Washington, DC: USEPA Off Pestic Toxic Substances (1980) (2) Urbach G; J

Chromatogr 404: 163-74 (1987) (3) Pellizzari ED et al; Bull Environ Contam Toxicol 28: 322-8 (1982)]**PEER REVIEWED**

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Environmental Fate/Exposure Summary:

Methyl ethyl ketone's production and use as a solvent for coatings, resins, rubbers, plastics, pharmaceuticals, adhesives and rubber cements will result in its release to the environment through various waste streams. Its use as a starting material or intermediate in the manufacture of chemical products will also lead to its release to the environment. **Methyl ethyl ketone** occurs naturally as a metabolic byproduct of plants and animals and is released into the atmosphere by volcanoes and forest fires. Based on an experimental vapor pressure of 91 mm Hg at 25 deg C, **methyl ethyl ketone** is expected to exist solely as a vapor in the ambient atmosphere. Vapor-phase **methyl ethyl ketone** is degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals with an estimated atmospheric half-life of about 14 days. This compound is also expected to undergo photolysis in the atmosphere by natural sunlight. Photochemical degradation of **methyl ethyl ketone** by natural sunlight is expected to occur at approximately 1/5 the rate of degradation by photochemically produced hydroxy radicals. **Methyl ethyl ketone** is expected to have very high mobility in soils based upon measured Koc values of 29 and 34 obtained in silt loams. Volatilization from dry soil surfaces is expected based upon the vapor pressure of this compound. Volatilization from moist soil surfaces is also expected based upon the measured Henry's Law constant of 4.7X10-5 atm-cu m/mol. The volatilization half-life of **methyl ethyl ketone** from silt and sandy loams was measured as 4.9 days. This compound is expected to biodegrade under aerobic and anaerobic conditions. In water, **methyl ethyl ketone** is not expected to adsorb to suspended solids or sediment based upon its measured Koc values. Volatilization from water surfaces is expected to be an important environmental fate process given its Henry's Law constant. Estimated half-lives for a model river and model lake are 19 and 197 hours, respectively. Bioconcentration in aquatic organisms is considered low based upon an estimated BCF value of 1. Occupational exposure may be through inhalation and dermal contact with this compound at workplaces where **methyl ethyl ketone** is produced or used. The general population may be exposed to **methyl ethyl ketone** through the use of commercially available products containing this compound such as paints, adhesives, and rubber cements. Exposure will also arise from inhalation of ambient air and ingestion of drinking water and food that contains **methyl ethyl ketone. (**SRC)

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Natural Pollution Sources:

Methyl ethyl ketone occurs naturally as a metabolic byproduct of plants and animals and is released into the atmosphere by volcanoes and forest fires(1).

[(1) Graedel TE et al; Atmospheric Chemical Compounds. NY,NY: Academic Press p. 263 (1986)]**PEER REVIEWED**

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Artificial Pollution Sources:

Methyl ethyl ketone's production and use as a solvent for coatings, resins, rubbers, plastics, pharmaceuticals, adhesives and rubber cements(1-3) will result in its release to the environment through various waste streams(SRC). Its use as a starting material or intermediate in the manufacture of chemical products(2,3) will also lead to its release to the environment(SRC).
[(1) Budvari S; Merck Index, 12th ed, Whitehouse Station,NJ: Merck & Co. p. 1773 (1996) (2) Browning E; Toxicity and Metabolism of Industrial Solvents. NY,NY: American Elsevier (1965) (3) Lewis RJ Sr ed; Hawley's Condensed Chemical Dictionary. 12th ed NY,NY: Van Nostrand Rheinhold Co p. 768 (1993)]**PEER REVIEWED**

Water pollution: Polyvinyl chloride pipe cement used for joint connection caused 4.5 ppm, 6 months after polyvinyl chloride pipe installation and 2.2 ppm after 8 months (at equilibrium condition-reached in about 48 hr).
[Verschueren, K. Handbook of Environmental Data of Organic Chemicals. 2nd ed. New York, NY: Van Nostrand Reinhold Co., 1983. 851]**PEER REVIEWED**

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Environmental Fate:

TERRESTRIAL FATE: Measured Koc values of 29 and 34 were obtained for **methyl ethyl ketone** in silt loams(1). Based on a recommended classification scheme(2), **methyl ethyl ketone** is expected to have very high mobility in soil(SRC). Volatilization of **methyl ethyl ketone** from dry soil surfaces is expected based upon an experimental vapor pressure of 91 mm Hg at 25 deg C(3). Volatilization from moist soil surfaces(SRC) is also expected given the measured Henry's Law constant of 4.7X10-5 atm-cu m/mole(4). The volatilization half-life of **methyl ethyl ketone** from silt and sandy loams was measured as 4.9 days(5). **Methyl ethyl ketone** is expected to biodegrade under both aerobic and anaerobic conditions as indicated by numerous screening tests(6-9).
[(1) Walton BT et al; J Environ Qual 21: 552-58 (1992) (2) Swann RL et al; Res Rev 85: 23 (1983) (3) Alarie Y et al; Toxicol Appl Pharmacol 134: 92-99 (1995) (4) Bhattacharaya SK et al; Water Res 30: 3099-3105 (1996) (5) Anderson TA et al; J Environ Qual 20: 420-24 (1991) (6) Bridie Al, et al; Water Res 13: 627-30 (1979) (7) Price KS et al; J Water Pollut Control Fed 46: 63-77 (1974) (8) Bhattacharaya SK et al; Wat Res 30: 3099-3105 (1996) (9) Suflita JM, Mormile MR; Environ Sci Technol 27: 976-78 (1993)]**PEER REVIEWED**

AQUATIC FATE: Based on experimental Koc values of 29 and 34 obtained in silt loams(1), and a recommended classification scheme(2), **methyl ethyl ketone** is not expected to adsorb to suspended solids and sediment in water(SRC). **Methyl ethyl ketone** is expected to volatilize from water surfaces(3,SRC) based on the measured Henry's Law constant of 4.7X10-5 atm-cu m/mole(4). Estimated half-lives for a model river and model lake are 19 and 197, hours respectively(3,SRC). Biodegradation of this compound is expected based upon numerous screening tests(5-8). According to a classification scheme(9), an estimated BCF value of 1(3,SRC), from an experimental log Kow of 0.29(10,SRC), suggests that bioconcentration in aquatic organisms is low(SRC).
[(1) Walton BT et al; J Environ Qual 21: 552-58 (1992) (2) Swann RL et al; Res Rev 85: 23 (1983) (3) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington DC: Amer Chem Soc pp. 4-9 (1990) (4) Bhattacharaya SK et al; Water Res 30: 3099-3105 (1996) (5) Bridie Al, et al; Water Res 13: 627-30 (1979) (6) Price KS et al; J Water Pollut Control Fed 46: 63-77 (1974) (7) Bhattacharaya SK et al; Wat Res 30: 3099-3105 (1996) (8) Suflita JM, Mormile MR; Environ Sci Technol 27: 976-78 (1993) (9) Franke C et al; Chemosphere 29: 1501-14 (1994) (10) Hansch C et al; Exploring QSAR Hydrophobic, Electronic and Stearic Constants Washington,DC: Amer Chem Soc (1995)]**PEER REVIEWED**

ATMOSPHERIC FATE: According to a model of gas/particle partitioning of semivolatile organic compounds in the atmosphere(1), **methyl ethyl ketone,** which has an experimental vapor pressure of 91 mm Hg at 25 deg C(2), will exist solely as a vapor in the ambient atmosphere. Vapor-phase **methyl ethyl ketone** is degraded in the atmosphere by reaction with photochemically-produced hydroxyl

radicals(SRC); the half-life for this reaction in air is estimated to be about 14(3,SRC) days. **Methyl ethyl ketone** is also expected to undergo photodecomposition in the atmosphere by natural sunlight(4,5). Photochemical degradation of **methyl ethyl ketone** by natural sunlight is expected to occur at approximately 1/5 the rate of degradation by photochemically produced hydroxyl radicals(5).
[(1) Bidleman TF; Environ Sci Technol 22: 361-367 (1988) (2) Alarie Y et al; Toxicol Appl Pharmacol 134: 92-99 (1995) (3) Atkinson R; J Phys Chem Ref Data (1989) (4) Raber W et al; pp. 364-70 in Phys Chem Behav Atmos Pollut 5th ed Restelli G, Angeletti G eds, Kluwer: Dordecht, Netherlands (1990) (5) Altshuller AP; J Atmos Chem 13: 155-82 (1991)]**PEER REVIEWED**

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Environmental Biodegradation:

Methyl ethyl ketone (MEK) is readily oxidized by microorganisms in activated sludge following selection and/or adaptation, with over 80% being removed in 24 hr. Metabolism in unacclimated sludges is slow.

[USEPA; Methyl Ethyl Ketone III: Exposure Aspects USEPA Contract No. 68-01-6147 (1981)]**PEER REVIEWED**

Biological oxygen demand (BOD) after 5 days @ 20 deg C: 1.515-1.92; 2.24 (std dilution technique, normal sewage seed); 5.3 (Dutch std test method); 1.81 (@ 10 mg/l, unadapted sewage, 1 days lag period).

[Verschueren, K. Handbook of Environmental Data of Organic Chemicals. 2nd ed. New York, NY: Van Nostrand Reinhold Co., 1983. 851]**PEER REVIEWED**

Chemical oxygen demand (COD): 2.20-2.31; 5.3 (Dutch std test method); theoretical oxygen demand (ThOD): 2.44; permanganate test value: 0.29.

[Verschueren, K. Handbook of Environmental Data of Organic Chemicals. 2nd ed. New York, NY: Van Nostrand Reinhold Co., 1983. 851]**PEER REVIEWED**

Using standard BOD and COD dilution techniques and a sewage inoculum, a theoretical BOD of 83% and a theoretical COD of 95% was reported over a 5 day incubation period(1). The percent theoretical BOD of **methyl ethyl ketone** in freshwater was reported as 76%, 82%, 84% and 89% over 5, 10 15 and 20 day incubation periods respectively(2). The percent theoretical BOD of **methyl ethyl ketone** in synthetic saltwater was reported as 32%, 62%, 63% and 69% over 5, 10 15 and 20 day incubation periods respectively(2). 92-95% biodegradation was reported when 0.25 mg/l of **methyl ethyl ketone** was fed through an activated sludge from a wastewater treatment plant over a 3 week incubation period(3). The percent theoretical methane recovery of **methyl ethyl ketone** in an anaerobic aquifer was 89% over a 3 week incubation period following a 15 day acclimation period(4).

[(1) Bridie Al, et al; Water Res 13: 627-30 (1979) (2) Price KS et al; J Water Pollut Control Fed 46: 63-77 (1974) (3) Bhattacharaya SK et al; Wat Res 30: 3099-3105 (1996) (4) Suflita JM, Mormile MR; Environ Sci Technol 27: 976-78 (1993)]**PEER REVIEWED**

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Environmental Abiotic Degradation:

The rate constant for the vapor-phase reaction of **methyl ethyl ketone** with photochemically-produced hydroxyl radicals has been measured as 1.15X10-12 cu cm/molecule-sec at 25 deg C(1). This corresponds to an atmospheric half-life of about 14 days at an atmospheric concn of 5.0X10+5 hydroxyl radicals per cu cm(1,SRC). **Methyl ethyl ketone** is also expected to undergo photodecomposition in the atmosphere by natural sunlight(2,3). Based on the actinic fluxes within the planet boundary layer, along with an estimated quantum yield and absorption cross section, the rate of photodissociation of **methyl ethyl ketone** by natural sunlight is approximately 1/5 the rate of dissociation by hydroxyl radicals(3). This compound is not expected to undergo hydrolysis in the environment due to a lack of functional groups which hydrolyze(SRC).

[(1) Atkinson R; J Phys Chem Ref Data (1989) (2) Raber W et al; pp. 364-70 in Phys Chem Behav Atmos Pollut 5th ed Restelli G, Angeletti G eds, Kluwer: Dordecht, Netherlands (1990) (3) Altshuller AP; J Atmos Chem 13: 155-82 (1991)]**PEER REVIEWED**

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Environmental Bioconcentration:

An estimated BCF value of 1 was calculated for **methyl ethyl ketone(**SRC), using an experimental log Kow of 0.29(1) and a recommended regression-derived equation(2). According to a classification scheme(3), this BCF value suggests that bioconcentration in aquatic organisms is low(SRC).
[(1) Hansch C et al; Exploring QSAR Hydrophobic, Electronic and Stearic Constants Washington DC: Amer Chem Soc (1995) (2) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington DC: Amer Chem Soc pp. 5-4, 5-10 (1990) (3) Franke C et al; Chemosphere 29: 1501-14 (1994)]**PEER REVIEWED**

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Soil Adsorption/Mobility:

Measured Koc values of 29 and 34 were obtained for **methyl ethyl ketone** in silt loams(1). Based on a recommended classification scheme(2), **methyl ethyl ketone** is expected to have very high mobility in soil(SRC).

[(1) Walton BT et al; J Environ Qual 21: 552-58 (1992) (2) Swann RL et al; Res Rev 85: 23 (1983)]**PEER REVIEWED**

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Volatilization from Water/Soil:

The Henry's Law constant for **methyl ethyl ketone** was measured as 4.7X10-5 atm-cu m/mole(SRC) at 25 deg C(1). This value indicates that **methyl ethyl ketone** will volatilize from water surfaces(2,SRC). Based on this Henry's Law constant, the volatilization half-life from a model river (1 m deep, flowing 1 m/sec, wind velocity of 3 m/sec) is estimated as approximately 19 hours(2,SRC). The volatilization half-life from a model lake (1 m deep, flowing 0.05 m/sec, wind velocity of 0.5 m/sec) is estimated as approximately 197 hours(2,SRC). **Methyl ethyl ketone** is expected to volatilize from dry soil surfaces given its experimental vapor pressure of 91 mm Hg at 25 deg C(3,SRC). The volatilization half-life of **methyl ethyl ketone** from silt and sandy loams was measured as 4.9 days(4).
[(1) Bhattacharaya SK et al; Water Res 30: 3099-3105 (1996) (2) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington DC: Amer Chem Soc pp. 15-1 to 15-29 (1990) (3) Alarie Y et al; Toxicol Appl Pharmacol 134: 92-99 (1995) (4) Anderson TA et al; J Environ Qual 20: 420-24 (1991)]**PEER REVIEWED**

METHYL ETHYL KETONE

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For other data, click on the Table of Contents

Environmental Water Concentrations:

DRINKING WATER: A Federal survey of public groundwater supplies detected **methyl ethyl ketone** in less than 5% of the samples(1). **Methyl ethyl ketone** was identified, not quantified, in drinking water supplies from 7 cities from varied sources and with different types of pollutant sources(2-4).
[(1) Dyksen JE, Hess AF III; J Amer Water Works Assoc 74: 394-403 (1982) (2) Coleman WE et al; pp. 305-207 in Analysis and Identification of Organic Substances in Water. Keith L ed Ann Arbor, MI Ann Arbor Press (1976) (3) Scheeman MA et al; Biomed Mass Spectrom 4: 209-11 (1974) (4) USEPA; New Orleans Area Water Supply Study. Draft Analytical Report by the Lower Mississippi River Facility, Slidell (1974)]**PEER REVIEWED**

GROUNDWATER: **Methyl ethyl ketone** was detected in groundwater at a coal strip-mine in Ohio at a concn of 650 mg/l(1). **Methyl ethyl ketone** was identified, not quantified, in on-site and off-site groundwater near a landfill in New Jersey(2). **Methyl ethyl ketone** was detected in the groundwater of a coal strip-mine in Lackawanne, PA at a maximum concn of 29,000 ppb(3). **Methyl ethyl ketone** was detected at an average concn of 12 ug/l in the groundwater of 19 solid waste disposal facilities in Wisconsin(4) and in the range of 0-91 ug/l in the groundwater of a landfill located in New Castle, DE(5). **Methyl ethyl ketone** was detected at an average concn of 60 ug/l in the groundwater of a chemical manufacturing facility in Alabama(6).
[(1) USEPA; Superfund Record of Decision : Summit National Site, Deerfield OH. USEPA/ROD/R85-88/068 (1988) (2) USEPA; Superfund Record of Decision: Lipari Landfill Mantau Township, NJ. USEPA/ROD/RO2-88/074 (1988) (3) ATSDR; Health assessment for Beacon Heights Landfill National Priorities List (NPL) Site, Beacon Falls, Connecticut, Region 1. CERCLIS NO. CTD001145671. Agency for Toxic Substances and Disease Registry PB90-135971 (1990) (4) Battista JR, Connelly JP; VOC contamination at selected Wisconsin landfills - sampling results and policy implications. Wisc Dept of Natural Resources, Madison, WI. Publ-SW-094 (1989) (5) ATSDR; Health assessment for Tybouts Corner land (Tybouts) National Priorities List (NPL) site, Wilmington, New Castle County, Deleware, Region 3. CERCLIS NO. DED000606079. Agency for Toxic Substances and Disease Registry PB90-144387 (1989) (6) USEPA; Superfund Record of Decision: Ciba-Geigy (Mcintosh Plant), AL. USEPA/ROD/R04-89/056 (1989)]**PEER REVIEWED**

SURFACE WATER: **Methyl ethyl ketone** was identified, not quantified, in the Black River in Tuscaloosa, AL(1) and Newark Bay, NJ(2). **Methyl ethyl ketone** was detected in the Potomac River at a concn of less than 40 ug/l(3). **Methyl ethyl ketone** was detected in a creek in New Castle, DE near a landfill at concns of 0-11,000 ug/l(4).
[(1) Berstch W et al; J Chromatog 112: 701-18 (1975) (2) Gunster DG et al; Environ Pollut 82: 245-53 (1993) (3) Hall LWJR et al; Aquat

Toxicol 10: 73-99 (1987) (4) ATSDR; Health assessment for Tybouts Corner land (Tybouts) National Priorities List (NPL) site, Wilmington, New Castle County, Deleware, Region 3. Agency for Toxic Substances and Disease Registry PB90-144387 (1989)]**PEER REVIEWED**

RAIN/SNOW: An unspecified concn of **methyl ethyl ketone** was detected in the rainfall in Japan(1). **Methyl ethyl ketone** was detected at concns of 0-0.47 ppb in the clouds in California and as trace amounts in fog-ice(2). **Methyl ethyl ketone** was detected in clouds (1,390 ng/l) and rainfall (139 ng/l) at a state park in North Carolina(3).
[(1) Kato T et al; Yokohama Kokuritsu Daigaku Kankyo Kagaku Kenkyu Senta Kiyo 6: 11-20 (1980) (2) Grosjean D, Wright B; Atmos Environ 17: 2093-6 (1983) (3) Aneja VP et al; J Air Waste Manage Assoc 43: 1239-44 (1993)]**PEER REVIEWED**

METHYL ETHYL KETONE

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Effluent Concentrations:

Methyl ethyl ketone was detected in the leachate of several municipal landfills at concns between 110-6,600 ug/l(1). **Methyl ethyl ketone** was detected in the leachate of a sand and gravel pit near Utica, NY at a concn of 540 ug/l(2). **Methyl ethyl ketone** was detected in the leachate of an industrial landfill (53 mg/l) and a municipal landfill (0.11-27 mg/l)(3).
[(1) Christensen TH et al; Crit Rev Environ Sci Technol 24: 119-202 (1994) (2) USEPA; Superfund Record of Decision: Ludlow Sand and Gravel Site, Town of Paris Oneida County, NY USEPA/ROD/R02-88/067 (1988) (3) Brown KW, Donnelly KC; Haz Waste Haz Mater 5: 1-30 (1988)]**PEER REVIEWED**

Methyl ethyl ketone was detected in the effluent of a municipal landfill in Quebec, Ontario at concns of 5,200 ppb and 3092 ppb(1). **Methyl ethyl ketone** was identified, not quantified in the emissions of a waste incinerator in West Germany(2), automobiles(3) and common household waste(4-7). **Methyl ethyl ketone** was detected in the effluent from a solid waste composting plant at concns of 130 ug/cu m (background air), 25,500 ug/cu m(tipping area), 1,400 ug/cu m (shredder), 9,400 ug/cu m(indoor air), 36,000 ug/cu m (digester), 4,300 ug/cu m(fresh compost), 8,700 ug/cu m(middle age compost), 14,500 ug/cu m(old compost) and 1,400 ug/cu m(curing region)(8). **Methyl ethyl ketone** was identified, not quantified, in the emissions of 200 out of 1,026 common household products(9). **Methyl ethyl ketone** was detected in the emissions of a photocopying machine at rates of less than 100 ug/hr to 380 ug/hr(10). **Methyl ethyl ketone** was detected at a concn of 974 ug/cu m in the emissions of active compost at a composting facility in Virginia(11).
[(1) Brosseau, Heitz M; Atmos Environ 25A: 1473-77 (1994) (2) Jay K, Stieglitz L; Chemosphere 30: 1249-60 (1995) (3) Harley RA et al; Environ Sci Technol 26: 2395-2408 (1992) (4) Wilkins CK, Larsen K; J High Resol Chromatogr 18: 373-77 (1995) (5) Wilkins K, Larsen K; Chemosphere 31: 3225-36 (1995) (6) Wilkins K, Larsen K; Chemosphere 32: 2049-55 (1996) (7) Wilkins K; Chemosphere 29: 47-53 (1994) (8) Eitzer BD; Environ Sci Technol 29: 896-902 (1995) (9) Sack TM et al; Atmos Environ 26A: 1063-70 (1992)(10) Leovic KW et al; J Air Waste Manage Assoc 46: 821-29 (1996) (11) Vandurme GP et al; Water Environ Res 64: 19-27 (1992)]**PEER REVIEWED**

METHYL ETHYL KETONE

CASRN: 78-93-3

For other data, click on the Table of Contents

Sediment/Soil Concentrations:

Methyl ethyl ketone was detected in the soil of a coal strip mine in Ohio at mean concns of 1,682 ug/kg (surface soil), 11,750 ug/kg (2-4 feet), 38,000 ug/kg (4-6 feet), 5,368 ug/kg (6-8 feet)(1). **Methyl ethyl ketone** was identified, not quantified, in the subsurface soil of a gravel mine in Tennessee(2). **Methyl ethyl ketone** was detected at an average concn of 1,615 ug/kg in the soil of an unauthorized hazardous waste disposal facility in New Jersey(3). **Methyl ethyl ketone** was detected at an average concn of 32 ug/kg in the soil of a waste disposal facility in Kansas(4).
[(1) USEPA; Superfund Record of Decision: Summit National Site, Deerfield OH. USEPA/ROD/R85-88/068 (1988) (2) USEPA; Superfund Record of Decision: Galloway Ponds Site, Galloway, TN. USEPA/ROD/R04-86/013 (1987) (3) USEPA; Superfund Record of Decision: Lang Property Pemberton Township, NJ USEPA/ROD/R02-86/031 (1987) (4) USEPA; Superfund Record of Decision: Doepke Disposal (Holliday), KS USEPA/ROD/R07-89/032 (1989)]**PEER REVIEWED**

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Atmospheric Concentrations:

The presence of solvents such as toluene, xylene, **methyl ethyl ketone,** and other similar products in the indoor air of an automobile body repair shop, an offset printing facility and the adjacent dwellings was monitored, and the individual exposure of the corresponding workers and residents was tested by biological monitoring of exhaled breath and by personal air sampling. The concentrations of solvents tested in the air of both sites surveyed were lower than prevailing Dutch Maximum Allowable Concentration levels. The levels of solvents recorded in the air of apartments situated on top of the facilities surveyed were significantly higher than the levels recorded in the surrounding dwellings. The levels of **methyl ethyl ketone,** toluene and xylene in personal air samples of employees at the body shop were 1.5 times higher than in ambient air. The level of toluene in alveolar air of residents living above the automobile repair shop was 50 percent higher than that recorded in spot samples. The levels of other solvents were equal to or lower than the detection level. At the offset printing facility, toluene, xylene, butylacetate, 2-ethoxyethanol and cyclohexanone in air and in personal air samples followed the same general pattern identified for the body shop. In a dwelling next to the shop and in an apartment on top of the shop, the concentrations ranged from 3 to 9 percent and 14 to 19 percent, respectively, of the levels recorded inside the facility itself.
[Verhoeff AP et al; Int Arch Occup Environ Health 59 (2): 153-63 (1987)]**PEER REVIEWED**

URBAN/SUBURBAN: **Methyl ethyl ketone** was detected at a mean concn of 1.5 ppb in Boston, MA(1). **Methyl ethyl ketone** was detected at mean concns of 1.35 ppb in Boston, MA, and 5.1 ppb in Houston, TX(2). The average concn of **methyl ethyl ketone** at 25 urban locations in the US was 1.4 ug/cu m(3). **Methyl ethyl ketone** was detected at a mean concn of 1.67 ppb in Los Angeles, CA(4) and in the Caldecott Tunnel in San Francisco, CA at a concn of 1.67 mg/l(5). **Methyl ethyl ketone** was detected at average concns of 0.222-1.366 ppb in Grenoble, France(6). An average concn of 0.638 ppb of **methyl ethyl ketone** was obtained from 714 atmospheric samples in the US(7).
[(1) Reiss R et al; J Air Waste Manage Assoc 45: 811-22(1995) (2) Kelly TJ et al; Environ Sci Technol 27: 1146-53 (1993) (3) Kelly TJ et al; Ambient concn summaries for Clean Air Act. Title III. Hazardous Air Pollutants. USEPA Contract No 68-D80082 USEPA/600/R-94/090 (1993) (4) Grosjean E et al; Environ Sci Technol 30: 2687-2703 (1996) (5) Kirschstetter TW et al; Environ Sci Technol 30: 661-70 (1996) (6) Foster P et al; Pollut Atmos: 175-91 (1991) (7) Shah JJ, Heyerdahl EK; Environ Sci Technol 22: 1381-88 (1988)]**PEER REVIEWED**

RURAL/REMOTE: **Methyl ethyl ketone** was detected at an average concn of 2.40 ng/l in the air of a state park in North Carolina(1). **Methyl ethyl ketone** was detected at an average concn of 18 ug/cu m at rural locations in Canada(2) and concns of 1.8-3.3 ppb in a rural location in Louisiana(3).
[(1) Aneja VP et al; J Air Waste Manage Assoc 43: 1239-44 (1993) (2) Chan CC et al; J Air Waste Manage Assoc 40: 62-67 (1990) (3) Khalil MAK, Rasmussen RA; J Air Waste Manage Assoc 42: 810-13 (1992)]**PEER REVIEWED**

SOURCE AREAS: **Methyl ethyl ketone** was detected at a median concn of 64 parts per trillion and a range of 10-1,900 parts per trillion(1) in source dominated areas in New Jersey(1). **Methyl ethyl ketone** was detected at a concn of 94 ppm near a reclamation plant(2).
[(1) Brodzinsky R, Singh HB; Volatile Organic Chemicals in the Atmos SRI International Contract 68-02-3452 (1982) (2) Lande SS et al; Investigation of Selected Potential Environmental Contaminants: Ketonic Solvents 331 p USEPA 560/2-76-003 (1976)]**PEER REVIEWED**

INDOOR AIR: **Methyl ethyl ketone** was detected at an average concn of 17.8 ug/cu m at dwellings in Canada(1) and 2.4 ppb in buildings in Boston, MA(2). **Methyl ethyl ketone** was detected in 2 federal office buildings in Portland, OR at concns between 2.0 and 40.9 ug/cu m(3). Four indoor air samples in the US had average concns of MEK of 9.238 ppb(4).
[(1) Chan CC et al; J Air Waste Manage Assoc 40: 62-67 (1990) (2) Reiss R et al; J Air Waste Manage Assoc 45: 811-22 (1995) (3) Hodgeson AT et al; J Air Waste Manage Assoc 41: 1461-68 (1991) (4) Shah JJ, Heyerdahl EK; Environ Sci Technol 22: 1381-88 (1988)]**PEER REVIEWED**

METHYL ETHYL KETONE

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Food Survey Values:

NON-ALCOHOLIC BEVERAGES 70 PPM; ICE CREAM, ICES, ETC 270 PPM; CANDY 100 PPM; BAKED GOODS 100 PPM

[Fenaroli's Handbook of Flavor Ingredients. Volume 2. Edited, translated, and revised by T.E. Furia and N. Bellanca. 2nd ed. Cleveland: The Chemical Rubber Co., 1975. 59]**PEER REVIEWED**

Methyl ethyl ketone was detected in Swiss cheese (0.3 ppm) and cream (0.154-0.177 ppm)(1). **Methyl ethyl ketone** was identified, not quantified, in the volatiles of roasted barley, bread, honey, chicken, oranges, black tea, and rum(1), kiwi fruit(2), chickpea seeds(3), mutton, chicken and beef(4). **Methyl ethyl ketone** was detected at a concn of 1.83 ug/g in rotten mussels in Japan(5).

[(1) Lande SS et al; Investigation of Selected Potential Environmental Contaminants: Ketonic Solvents. 331 pp. USEPA 560/2-76-003 (1976) (2) Tatsuka K et al; J Food Sci 38: 2176-80 (1990) (3) Rembold H et al; J Agric Food Chem 37: 659-62 (1989) (4) Shahidi F et al; CRC Crit Rev Food Sci Nature 24: 141-243 (1986) (5) Yasuhara A; J Chromatogr 409: 251-58 (1987)]**PEER REVIEWED**

METHYL ETHYL KETONE

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Plant Concentrations:

32 samples of southern pea seed, Vigna unguiculata, were analyzed for volatiles. **Methyl ethyl ketone (**MEK) was found in all samples and the mean concn was 151 + or - 80 ppb (74 to 390 ppb).
[Fisher GS et al; J Agric Food Chem 27: 7-11 (1979)]**PEER REVIEWED**

Methyl ethyl ketone is emitted from pencil cedar, Zeravshan juniper, European firs and Evergreen cyprus(1). **Methyl ethyl ketone** was detected in 32 of 32 samples of southern pea seeds at a mean concn of 151 ppb(2).
[(1) Singh HB, Zimmerman PB; Adv Environ Sci Technol 24: 177-235 (1992) (2) Fisher GS et al; J Agric Food Chem 27: 7-11 (1979)]**PEER REVIEWED**

METHYL ETHYL KETONE

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Milk Concentrations:

Milk 0.077-0.079 ppm, milk fat 8 ppm(1).

[(1) Lande SS et al; Investigation of Selected Potential Environmental Contaminants: Ketonic Solvents p. 102 USEPA 560/2-76-003 (1976)]**PEER REVIEWED**

Methyl ethyl ketone was identified, not quantified in human milk samples in Bayonne, NJ(1) Pittsburgh, PA(1) Baton Rouge, LA(1) and Australia(2). **Methyl ethyl ketone** was identified, not quantified in 5 of 8 samples of human milk from 4 US urban areas(3).

[(1) Erickson MD et al; Acquisition and chemical analysis of mother's milk for selected toxic substances. USEPA-560/13-80-029. Washington, DC: USEPA Off Pestic Toxic Substances (1980) (2) Urbach G; J Chromatogr 404: 163-74 (1987) (3) Pellizzari ED et al; Bull Environ Contam Toxicol 28: 322-8 (1982)]**PEER REVIEWED**

METHYL ETHYL KETONE

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Environmental Standards & Regulations:

FIFRA Requirements:

Unless designated as an active ingredient in accordance with paragraph (b) or (c) of this section, this substance, when used in antimicrobial products, is considered inert, having no independent pesticidal activity. The percentage of such an ingredient shall be included on the label in the total percentage of inert ingredients.
[40 CFR 162.60 (7/1/88)]**PEER REVIEWED**

Methyl ethyl ketone is exempted from the requirement of a tolerance when used as a solvent, cosolvent in accordance with good agricultural practice as inert (or occasionally active) ingredients in pesticide formulations applied to growing crops only.
[40 CFR 180.1001(d) (7/1/96)]**PEER REVIEWED**

Acceptable Daily Intakes:

... An Acceptable Daily Intake (ADI), defined as the amount of a chemical to which humans can be exposed on a daily basis over an extended period of time (usually a lifetime) without suffering a deleterious effect, for **methyl ethyl ketone** is 3.2 mg/day for oral exposure. ...
[USEPA; Health and Environmental Effects Profile for Methyl Ethyl Ketone p.80 (1988) EPA/600/X-85/363]**PEER REVIEWED**

TSCA Requirements:

Pursuant to section 8(d) of TSCA, EPA promulgated a model Health and Safety Data Reporting Rule. The section 8(d) model rule requires manufacturers, importers, and processors of listed chemical substances and mixtures to submit to EPA copies and lists of unpublished health and safety studies. **Methyl ethyl ketone** is included on this list.
[40 CFR 716.120 (7/1/96)]**PEER REVIEWED**

CERCLA Reportable Quantities:

Persons in charge of vessels or facilities are required to notify the National Response Center (NRC) immediately, when there is a release of this designated hazardous substance, in an amount equal to or greater than its reportable quantity of 5000 lb or 2270 kg. The toll free number of the NRC is (800) 424-8802; In the Washington D.C. metropolitan area (202) 426-2675. The rule for determining when notification is required is stated in 40 CFR 302.4 (section IV. D.3.b).
[40 CFR 302.4 (7/1/96)]**PEER REVIEWED**

RCRA Requirements:

U159; As stipulated in 40 CFR 261.33, when 2-**butanone**, as a commercial chemical product or manufacturing chemical intermediate or an off-specification commercial chemical product or a manufacturing chemical intermediate, becomes a waste, it must be managed according to Federal and/or

State hazardous waste regulations. Also defined as a hazardous waste is any residue, contaminated soil, water, or other debris resulting from the cleanup of a spill, into water or on dry land, of this waste. Generators of small quantities of this waste may qualify for partial exclusion from hazardous waste regulations (40 CFR 261.5).
[40 CFR 261.33 (7/1/96)]**PEER REVIEWED**

F005; When **methyl ethyl ketone** is a spent solvent, it is classified as a hazardous waste from a nonspecific source (F005), as stated in 40 CFR 261.31, and must be managed according to State and/or Federal hazardous waste regulations.
[40 CFR 261.31 (7/1/96)]**PEER REVIEWED**

Atmospheric Standards:

This action promulgates standards of performance for equipment leaks of Volatile Organic Compounds (VOC) in the Synthetic Organic Chemical Manufacturing Industry (SOCMI). The intended effect of these standards is to require all newly constructed, modified, and reconstructed SOCMI process units to use the best demonstrated system of continuous emission reduction for equipment leaks of VOC, considering costs, non air quality health and environmental impact and energy requirements. **Methyl ethyl ketone** is produced, as an intermediate or final product, by process units covered under this subpart.
[40 CFR 60.489 (7/1/87)]**PEER REVIEWED**

Listed as a hazardous air pollutant (HAP) generally known or suspected to cause serious health problems. The Clean Air Act, as amended in 1990, directs EPA to set standards requiring major sources to sharply reduce routine emissions of toxic pollutants. EPA is required to establish and phase in specific performance based standards for all air emission sources that emit one or more of the listed pollutants. **Methyl ethyl ketone** is included on this list.
[Clean Air Act as amended in 1990, Sect. 112 (b) (1) Public Law 101-549 Nov. 15, 1990]**QC REVIEWED**

State Drinking Water Guidelines:

(AZ) ARIZONA 170 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

(FL) FLORIDA 4,200 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

(MA) MASSACHUSETTS 350 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

(ME) MAINE 170 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis

Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

(MN) MINNESOTA 4000 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

(NC) NORTH CAROLINA 170 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

(NH) NEW HAMPSHIRE 170 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

(NJ) NEW JERSEY 270 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

(WI) WISCONSIN 460 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

FDA Requirements:

Methyl ethyl ketone is an indirect food additive for use only as a component of adhesives.
[21 CFR 175.105 (4/1/96)]**PEER REVIEWED**

Methyl ethyl ketone is an indirect food additive polymer for use as a basic component of single and repeated use food contact surfaces. Residue limit 0.1% by weight of finished packaging cellophane.
[21 CFR 177.1200 (4/1/96)]**PEER REVIEWED**

Methyl ethyl ketone is a food additive permitted for direct addition to food for human consumption as a synthetic flavoring substance and adjuvant in accordance with the following conditions: 1) the quantity added to food does not exceed the amount reasonably required to accomplish its intended physical, nutritive, or other technical effect in food, and 2) when intended for use in or on food it is of appropriate food grade and is prepared and handled as a food ingredient.
[21 CFR 172.515 (4/1/96)]**PEER REVIEWED**

Allowable Tolerances:

Methyl ethyl ketone is exempted from the requirement of a tolerance when used as a solvent, cosolvent in accordance with good agricultural practice as inert (or occasionally active) ingredients in pesticide formulations applied to growing crops only.
[40 CFR 180.1001(d) (7/1/96)]**PEER REVIEWED**

METHYL ETHYL KETONE

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FIFRA Requirements:

Unless designated as an active ingredient in accordance with paragraph (b) or (c) of this section, this substance, when used in antimicrobial products, is considered inert, having no independent pesticidal activity. The percentage of such an ingredient shall be included on the label in the total percentage of inert ingredients.
[40 CFR 162.60 (7/1/88)]**PEER REVIEWED**

Methyl ethyl ketone is exempted from the requirement of a tolerance when used as a solvent, cosolvent in accordance with good agricultural practice as inert (or occasionally active) ingredients in pesticide formulations applied to growing crops only.
[40 CFR 180.1001(d) (7/1/96)]**PEER REVIEWED**

METHYL ETHYL KETONE

CASRN: 78-93-3

For other data, click on the Table of Contents

Acceptable Daily Intakes:

... An Acceptable Daily Intake (ADI), defined as the amount of a chemical to which humans can be exposed on a daily basis over an extended period of time (usually a lifetime) without suffering a deleterious effect, for **methyl ethyl ketone** is 3.2 mg/day for oral exposure. ...
[USEPA; Health and Environmental Effects Profile for Methyl Ethyl Ketone p.80 (1988) EPA/600/X-85/363]**PEER REVIEWED**

METHYL ETHYL KETONE

CASRN: 78-93-3

For other data, click on the Table of Contents

TSCA Requirements:

Pursuant to section 8(d) of TSCA, EPA promulgated a model Health and Safety Data Reporting Rule. The section 8(d) model rule requires manufacturers, importers, and processors of listed chemical substances and mixtures to submit to EPA copies and lists of unpublished health and safety studies. **Methyl ethyl ketone** is included on this list.

[40 CFR 716.120 (7/1/96)]**PEER REVIEWED**

METHYL ETHYL KETONE

CASRN: 78-93-3

For other data, click on the Table of Contents

CERCLA Reportable Quantities:

Persons in charge of vessels or facilities are required to notify the National Response Center (NRC) immediately, when there is a release of this designated hazardous substance, in an amount equal to or greater than its reportable quantity of 5000 lb or 2270 kg. The toll free number of the NRC is (800) 424-8802; In the Washington D.C. metropolitan area (202) 426-2675. The rule for determining when notification is required is stated in 40 CFR 302.4 (section IV. D.3.b).
[40 CFR 302.4 (7/1/96)]**PEER REVIEWED**

METHYL ETHYL KETONE

CASRN: 78-93-3

For other data, click on the Table of Contents

RCRA Requirements:

U159; As stipulated in 40 CFR 261.33, when 2-**butanone**, as a commercial chemical product or manufacturing chemical intermediate or an off-specification commercial chemical product or a manufacturing chemical intermediate, becomes a waste, it must be managed according to Federal and/or State hazardous waste regulations. Also defined as a hazardous waste is any residue, contaminated soil, water, or other debris resulting from the cleanup of a spill, into water or on dry land, of this waste. Generators of small quantities of this waste may qualify for partial exclusion from hazardous waste regulations (40 CFR 261.5).
[40 CFR 261.33 (7/1/96)]**PEER REVIEWED**

F005; When **methyl ethyl ketone** is a spent solvent, it is classified as a hazardous waste from a nonspecific source (F005), as stated in 40 CFR 261.31, and must be managed according to State and/or Federal hazardous waste regulations.
[40 CFR 261.31 (7/1/96)]**PEER REVIEWED**

METHYL ETHYL KETONE

CASRN: 78-93-3

For other data, click on the Table of Contents

Atmospheric Standards:

This action promulgates standards of performance for equipment leaks of Volatile Organic Compounds (VOC) in the Synthetic Organic Chemical Manufacturing Industry (SOCMI). The intended effect of these standards is to require all newly constructed, modified, and reconstructed SOCMI process units to use the best demonstrated system of continuous emission reduction for equipment leaks of VOC, considering costs, non air quality health and environmental impact and energy requirements. **Methyl ethyl ketone** is produced, as an intermediate or final product, by process units covered under this subpart.

[40 CFR 60.489 (7/1/87)]**PEER REVIEWED**

Listed as a hazardous air pollutant (HAP) generally known or suspected to cause serious health problems. The Clean Air Act, as amended in 1990, directs EPA to set standards requiring major sources to sharply reduce routine emissions of toxic pollutants. EPA is required to establish and phase in specific performance based standards for all air emission sources that emit one or more of the listed pollutants. **Methyl ethyl ketone** is included on this list.

[Clean Air Act as amended in 1990, Sect. 112 (b) (1) Public Law 101-549 Nov. 15, 1990]**QC REVIEWED**

METHYL ETHYL KETONE

CASRN: 78-93-3

For other data, click on the Table of Contents

State Drinking Water Guidelines:

(AZ) ARIZONA 170 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

(FL) FLORIDA 4,200 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

(MA) MASSACHUSETTS 350 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

(ME) MAINE 170 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

(MN) MINNESOTA 4000 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

(NC) NORTH CAROLINA 170 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

(NH) NEW HAMPSHIRE 170 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

(NJ) NEW JERSEY 270 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

(WI) WISCONSIN 460 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water

Standards and Guidelines (11/93)] **QC REVIEWED**

METHYL ETHYL KETONE

CASRN: 78-93-3

For other data, click on the Table of Contents

FDA Requirements:

Methyl ethyl ketone is an indirect food additive for use only as a component of adhesives.
[21 CFR 175.105 (4/1/96)]**PEER REVIEWED**

Methyl ethyl ketone is an indirect food additive polymer for use as a basic component of single and repeated use food contact surfaces. Residue limit 0.1% by weight of finished packaging cellophane.
[21 CFR 177.1200 (4/1/96)]**PEER REVIEWED**

Methyl ethyl ketone is a food additive permitted for direct addition to food for human consumption as a synthetic flavoring substance and adjuvant in accordance with the following conditions: 1) the quantity added to food does not exceed the amount reasonably required to accomplish its intended physical, nutritive, or other technical effect in food, and 2) when intended for use in or on food it is of appropriate food grade and is prepared and handled as a food ingredient.
[21 CFR 172.515 (4/1/96)]**PEER REVIEWED**

METHYL ETHYL KETONE

CASRN: 78-93-3

For other data, click on the Table of Contents

Allowable Tolerances:

Methyl ethyl ketone is exempted from the requirement of a tolerance when used as a solvent, cosolvent in accordance with good agricultural practice as inert (or occasionally active) ingredients in pesticide formulations applied to growing crops only.
[40 CFR 180.1001(d) (7/1/96)]**PEER REVIEWED**

METHYL ETHYL KETONE

CASRN: 78-93-3

For other data, click on the Table of Contents

Chemical/Physical Properties:

Molecular Formula:

C4-H8-O
PEER REVIEWED

Molecular Weight:

72.11
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 1037]**PEER REVIEWED**

Color/Form:

COLORLESS LIQUID
[Sax, N.I. Dangerous Properties of Industrial Materials. 6th ed. New York, NY: Van Nostrand Reinhold, 1984. 549]**PEER REVIEWED**

Odor:

ACETONE-LIKE ODOR
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 1037]**PEER REVIEWED**

Sweet, pleasant, pungent
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Moderately sharp, fragrant, mint- or acetone-like odor.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 94-116. Washington, D.C.: U.S. Government Printing Office, June 1994. 36]**PEER REVIEWED**

Taste:

Taste threshold: 3.00x10+1 ppm in milk (media and purity not specified)
[Fazzalari, F.A. (ed.). Compilation of Odor and Taste Threshold Values Data. ASTM Data Series DS 48A (Committee E-18). Philadelphia, PA: American Society for Testing and Materials, 1978. 24]**PEER REVIEWED**

Taste threshold: 5.00x10+1 ppm in milk (purity not specified)
[Fazzalari, F.A. (ed.). Compilation of Odor and Taste Threshold Values

Data. ASTM Data Series DS 48A (Committee E-18). Philadelphia, PA: American Society for Testing and Materials, 1978. 24]**PEER REVIEWED**

Boiling Point:

79.6 DEG C
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 1037]**PEER REVIEWED**

Melting Point:

-86 DEG C
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 1037]**PEER REVIEWED**

Critical Temperature & Pressure:

CRITICAL TEMP: 504.5 DEG F= 262.5 DEG C= 535.7 DEG K; CRITICAL PRESSURE: 603 PSIA= 41.0 ATM= 4.15 MN/SQ M
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Density/Specific Gravity:

0.805 AT 20 DEG C/4 DEG C
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 1037]**PEER REVIEWED**

Heat of Combustion:

-13,480 BTU/LB= -7491 CAL/G= -313.6X10+5 JOULES/KG
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Heat of Vaporization:

LATENT HEAT OF VAPORIZATION: 191 BTU/LB= 106 CAL/G= 4.44X10+5 JOULES/KG
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Octanol/Water Partition Coefficient:

Log Kow = 0.29
[Hansch, C., Leo, A., D. Hoekman. Exploring QSAR - Hydrophobic, Electronic, and Steric Constants. Washington, DC: American Chemical

Society., 1995. 9]**PEER REVIEWED**

Solubilities:

353,000 mg/l in water @ 10 deg C
[Verschueren, K. Handbook of Environmental Data on Organic Chemicals. 3rd ed. New York, NY: Van Nostrand Reinhold Co., 1996. 1281]**PEER REVIEWED**

SOL IN ALCOHOL, ETHER, ACETONE, & BENZENE
[Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 76th ed. Boca Raton, FL: CRC Press Inc., 1995-1996.,p. 3-101]**PEER REVIEWED**

190,000 mg/l in water @ 90 deg C
[Verschueren, K. Handbook of Environmental Data on Organic Chemicals. 3rd ed. New York, NY: Van Nostrand Reinhold Co., 1996. 1281]**PEER REVIEWED**

Spectral Properties:

MAX ABSORPTION (ALCOHOL): 273.5 NM (LOG E= 1.24); SADTLER REF NUMBER: 297 (IR, PRISM); 101 (IR, GRATING)
[Weast, R.C. (ed.). Handbook of Chemistry and Physics. 60th ed. Boca Raton, Florida: CRC Press Inc., 1979.,p. C-228]**PEER REVIEWED**

INDEX OF REFRACTION: 1.3814 @ 15 DEG C/D
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 1037]**PEER REVIEWED**

IR: 4788 (Coblentz Society Spectral Collection)
[Weast, R.C. and M.J. Astle. CRC Handbook of Data on Organic Compounds. Volumes I and II. Boca Raton, FL: CRC Press Inc. 1985.,p. V1 334]**PEER REVIEWED**

UV: 3-21 (Organic Electronic Spectral Data, Phillips et al, John Wiley & Sons, New York)
[Weast, R.C. and M.J. Astle. CRC Handbook of Data on Organic Compounds. Volumes I and II. Boca Raton, FL: CRC Press Inc. 1985.,p. V1 334]**PEER REVIEWED**

NMR: 76 (Varian Associates NMR Spectra Catalogue)
[Weast, R.C. and M.J. Astle. CRC Handbook of Data on Organic Compounds. Volumes I and II. Boca Raton, FL: CRC Press Inc. 1985.,p. V1 334]**PEER REVIEWED**

MASS: 68 (Atlas of Mass Spectral Data, John Wiley & Sons, New York)
[Weast, R.C. and M.J. Astle. CRC Handbook of Data on Organic Compounds. Volumes I and II. Boca Raton, FL: CRC Press Inc. 1985.,p. V1 334]**PEER REVIEWED**

Surface Tension:

24.6 dyne/cm @ 20 deg C
[Kirk-Othmer Encyclopedia of Chemical Technology. 4th ed. Volumes 1: New York, NY. John Wiley and Sons, 1991-Present.,p. V14 980]**PEER REVIEWED**

Vapor Density:

2.41 (Air= 1)
[Verschueren, K. Handbook of Environmental Data on Organic Chemicals. 3rd ed. New York, NY: Van Nostrand Reinhold Co., 1996. 1281]**PEER REVIEWED**

Vapor Pressure:

91 mm Hg at 25 deg C
[Alarie Y et al; Toxicol Appl Pharmacol 134: 92-99 (1995)]**PEER REVIEWED**

Relative Evaporation Rate:

EVAPORATION RATE: 2.7 (ETHER= 1)
[Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965. 421]**PEER REVIEWED**

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[Kirk-Othmer Encyclopedia of Chemical Technology. 4th ed. Volumes 1: New York, NY. John Wiley and Sons, 1991-Present.,p. V14 980]**PEER REVIEWED**

Other Chemical/Physical Properties:

CONSTANT BOILING MIXTURE WITH WATER, BP 73.4 DEG C, CONTAINS 88.7% **METHYL ETHYL KETONE (**MEK); SOLUBILITY OF WATER IN MEK IS 12.5% @ 25 DEG C
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 1037]**PEER REVIEWED**

SATURATED AIR CONCN IS 102,000 PPM @ 77.5 TORR, 20 DEG C
[American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices. 5th ed. Cincinnati, OH:American Conference of Governmental Industrial Hygienists, 1986. 395]**PEER REVIEWED**

HEAT OF SOLN (EST): -9 BTU/LB= -5 CAL/G= -0.2X10+5 JOULES/KG; RATIO OF SPECIFIC HEATS OF VAPOR (GAS): 1.075; REID VAPOR PRESSURE: 3.5 PSIA
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous

Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

CONVERSION FACTORS: 1 PPM= 2.94 MG/CU M; 1 MG/CU M= 0.340 PPM
[Verschueren, K. Handbook of Environmental Data on Organic Chemicals. 3rd ed. New York, NY: Van Nostrand Reinhold Co., 1996. 1282]**PEER REVIEWED**

Heat of fusion: 8.44 kJ/mole
[Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 76th ed. Boca Raton, FL: CRC Press Inc., 1995-1996.,p. 6-133]**PEER REVIEWED**

Coefficient of expansion= 0.00076/deg F; electrical conductivity= 1.0X10-7 ohms @ 25 deg C
[Flick, E.W. Industrial Solvents Handbook. 3rd ed. Park Ridge, NJ: Noyes Publications, 1985. 473]**PEER REVIEWED**

Partition coefficients at 37 deg C for **methyl ethyl ketone** into blood= 202; into oil= 263.
[Sato A, Nakajima T; Scand J Work Environ Health 13: 81-93 (1987)]**PEER REVIEWED**

It is lighter than water ... and may be expected to float while rapidly dissolving.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, D.C.: Assoc. of American Railroads,Hazardous Materials Systems (BOE), 1987. 452]**PEER REVIEWED**

Henry's Law constant = 4.7X10-5 atm-cu m/mol at 25 deg C
[Bhattacharaya SK et al; Water Res 30: 3099-3105 (1996)]**PEER REVIEWED**

METHYL ETHYL KETONE

CASRN: 78-93-3

For other data, click on the Table of Contents

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PEER REVIEWED

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Sweet, pleasant, pungent

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Moderately sharp, fragrant, mint- or acetone-like odor.

[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 94-116. Washington, D.C.: U.S. Government Printing Office, June 1994. 36]**PEER REVIEWED**

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Melting Point:

-86 DEG C

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METHYL ETHYL KETONE

CASRN: 78-93-3

For other data, click on the Table of Contents

Octanol/Water Partition Coefficient:

Log Kow = 0.29

[Hansch, C., Leo, A., D. Hoekman. Exploring QSAR - Hydrophobic, Electronic, and Steric Constants. Washington, DC: American Chemical Society., 1995. 9]**PEER REVIEWED**

METHYL ETHYL KETONE

CASRN: 78-93-3

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Solubilities:

353,000 mg/l in water @ 10 deg C

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SOL IN ALCOHOL, ETHER, ACETONE, & BENZENE

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MAX ABSORPTION (ALCOHOL): 273.5 NM (LOG E= 1.24); SADTLER REF NUMBER: 297 (IR, PRISM); 101 (IR, GRATING)
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IR: 4788 (Coblentz Society Spectral Collection)
[Weast, R.C. and M.J. Astle. CRC Handbook of Data on Organic Compounds. Volumes I and II. Boca Raton, FL: CRC Press Inc. 1985.,p. V1 334]**PEER REVIEWED**

UV: 3-21 (Organic Electronic Spectral Data, Phillips et al, John Wiley & Sons, New York)
[Weast, R.C. and M.J. Astle. CRC Handbook of Data on Organic Compounds. Volumes I and II. Boca Raton, FL: CRC Press Inc. 1985.,p. V1 334]**PEER REVIEWED**

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METHYL ETHYL KETONE

CASRN: 78-93-3

For other data, click on the Table of Contents

Surface Tension:

24.6 dyne/cm @ 20 deg C

[Kirk-Othmer Encyclopedia of Chemical Technology. 4th ed. Volumes 1: New York, NY. John Wiley and Sons, 1991-Present.,p. V14 980]**PEER REVIEWED**

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Vapor Density:

2.41 (Air= 1)

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METHYL ETHYL KETONE

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Vapor Pressure:

91 mm Hg at 25 deg C

[Alarie Y et al; Toxicol Appl Pharmacol 134: 92-99 (1995)]**PEER REVIEWED**

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Relative Evaporation Rate:

EVAPORATION RATE: 2.7 (ETHER= 1)
[Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965. 421]**PEER REVIEWED**

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0.41 mPa.s @ 20 deg C

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[American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices. 5th ed. Cincinnati, OH:American Conference of Governmental Industrial Hygienists, 1986. 395]**PEER REVIEWED**

HEAT OF SOLN (EST): -9 BTU/LB= -5 CAL/G= -0.2X10+5 JOULES/KG; RATIO OF SPECIFIC HEATS OF VAPOR (GAS): 1.075; REID VAPOR PRESSURE: 3.5 PSIA
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Coefficient of expansion= 0.00076/deg F; electrical conductivity= 1.0X10-7 ohms @ 25 deg C
[Flick, E.W. Industrial Solvents Handbook. 3rd ed. Park Ridge, NJ: Noyes Publications, 1985. 473]**PEER REVIEWED**

Partition coefficients at 37 deg C for **methyl ethyl ketone** into blood= 202; into oil= 263.
[Sato A, Nakajima T; Scand J Work Environ Health 13: 81-93 (1987)]**PEER REVIEWED**

It is lighter than water ... and may be expected to float while rapidly dissolving.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, D.C.: Assoc. of American Railroads,Hazardous Materials Systems (BOE), 1987. 452]**PEER REVIEWED**

Henry's Law constant = 4.7X10-5 atm-cu m/mol at 25 deg C
[Bhattacharaya SK et al; Water Res 30: 3099-3105 (1996)]**PEER

REVIEWED**

METHYL ETHYL KETONE

CASRN: 78-93-3

For other data, click on the Table of Contents

Chemical Safety & Handling:

DOT Emergency Guidelines:

Fire or explosion: HIGHLY FLAMMABLE: Will be easily ignited by heat, sparks or flames. Vapors may form explosive mixtures with air. Vapors may travel to source of ignition and flash back. Most vapors are heavier than air. They will spread along ground and collect in low or confined areas (sewers, basements, tanks). Vapor explosion hazard indoors, outdoors or in sewers. Some may polymerize (P) explosively when heated or involved in a fire. Runoff to sewer may create fire or explosion hazard. Containers may explode when heated. Many liquids are lighter than water.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-127]**PEER REVIEWED**

Health: Inhalation or contact with material may irritate or burn skin and eyes. Fire may produce irritating, corrosive and/or toxic gases. Vapors may cause dizziness or suffocation. Runoff from fire control may cause pollution.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-127]**PEER REVIEWED**

Public safety: CALL Emergency Response Telephone Number. ... Isolate spill or leak area immediately for at least 25 to 50 meters (80 to 160 feet) in all directions. Keep unauthorized personnel away. Stay upwind. Keep out of low areas. Ventilate closed spaces before entering.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-127]**PEER REVIEWED**

Protective clothing: Wear positive pressure self-contained breathing apparatus (SCBA). Structural firefighters' protective clothing will only provide limited protection.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs

Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-127]**PEER REVIEWED**

Evacuation: Large spill: Consider initial downwind evacuation for at least 300 meters (1000 feet). Fire: If tank, rail car or tank truck is involved in a fire, ISOLATE for 800 meters (1/2 mile) in all directions; also, consider initial evacuation for 800 meters (1/2 mile) in all directions.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-127]**PEER REVIEWED**

Fire: CAUTION: All these products have a very low flash point: Use of water spray when fighting fire may be inefficient. Small fires: Dry chemical, CO2, water spray or alcohol-resistant foam. Large fires: Water spray, fog or alcohol-resistant foam. Do not use straight streams. Move containers from fire area if you can do it without risk. Fire involving tanks or car/trailer loads: Fight fire from maximum distance or use unmanned hose holders or monitor nozzles. Cool containers with flooding quantities of water until well after fire is out. Withdraw immediately in case of rising sound from venting safety devices or discoloration of tank. ALWAYS stay away from the ends of tanks. For massive fire, use unmanned hose holders or monitor nozzles; if this is impossible, withdraw from area and let fire burn.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-127]**PEER REVIEWED**

Spill or leak: ELIMINATE all ignition sources (no smoking, flares, sparks or flames in immediate area). All equipment used when handling the product must be grounded. Do not touch or walk through spilled material. Stop leak if you can do it without risk. Prevent entry into waterways, sewers, basements or confined areas. A vapor suppressing foam may be used to reduce vapors. Absorb or cover with dry earth, sand or other non-combustible material and transfer to containers. Use clean non-sparking tools to collect absorbed material. Large spills: Dike far ahead of liquid spill for later disposal. Water spray may reduce vapor; but may not prevent ignition in closed spaces.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-127]**PEER REVIEWED**

First aid: Move victim to fresh air. Call emergency medical care. Apply artificial respiration if victim is not breathing. Administer oxygen if breathing is difficult. Remove and isolate contaminated clothing and shoes. In case of contact with substance, immediately flush skin or eyes with running water for at least 20 minutes. Wash skin with soap and water. Keep victim warm and quiet. Ensure that medical personnel are aware of the material(s) involved, and take precautions to protect themselves.

[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-127]**PEER REVIEWED**

Odor Threshold:

Odor low= 0.7375 mg/cu m; Odor high= 147.5 mg/cu m.
[Ruth JH; Am Ind Hyg Assoc J 47: A-142-51 (1986)]**PEER REVIEWED**

Detection limit in water: 5.00x10+1 ppm (purity not specified)
[Fazzalari, F.A. (ed.). Compilation of Odor and Taste Threshold Values Data. ASTM Data Series DS 48A (Committee E-18). Philadelphia, PA: American Society for Testing and Materials, 1978. 24]**PEER REVIEWED**

Recognition in air: 1.00x10+1 ppm (chemically pure)
[Fazzalari, F.A. (ed.). Compilation of Odor and Taste Threshold Values Data. ASTM Data Series DS 48A (Committee E-18). Philadelphia, PA: American Society for Testing and Materials, 1978. 24]**PEER REVIEWED**

Detection limit in air: 2.00x10+1 ppm (purity not specified)
[Fazzalari, F.A. (ed.). Compilation of Odor and Taste Threshold Values Data. ASTM Data Series DS 48A (Committee E-18). Philadelphia, PA: American Society for Testing and Materials, 1978. 24]**PEER REVIEWED**

Recognition in air: 5.50x10+1 ppm (purity not specified)
[Fazzalari, F.A. (ed.). Compilation of Odor and Taste Threshold Values Data. ASTM Data Series DS 48A (Committee E-18). Philadelphia, PA: American Society for Testing and Materials, 1978. 24]**PEER REVIEWED**

Skin, Eye and Respiratory Irritations:

High atm concn ... are irritating to the eyes, nose, and throat ... .
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1748]**PEER REVIEWED**

Vapor is irritating to human mucous membranes and conjuntivae @ 200 ppm after 15 min ... .
[Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984.,p. II-185]**PEER REVIEWED**

Fire Potential:

Highly flammable liquid.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 2239]**PEER REVIEWED**

NFPA Hazard Classification:

Health: 1. 1= Materials that, on exposure, would cause irritation, but only minor residual injury, including those requiring the use of an approved air-purifying respirator. These materials are only slightly hazardous to health and breathing protection is needed.
[National Fire Protection Guide. Fire Protection Guide on Hazardous Materials. 10 th ed. Quincy, MA: National Fire Protection Association, 1991.,p. 325M-69]**PEER REVIEWED**

Flammability: 3. 3= Includes Class IB and IC flammable liquids and materials that can be easily ignited under almost all normal temp conditions. Water may be ineffective in controlling or extinguishing fires in such materials.
[National Fire Protection Guide. Fire Protection Guide on Hazardous Materials. 10 th ed. Quincy, MA: National Fire Protection Association, 1991.,p. 325M-69]**PEER REVIEWED**

Reactivity: 0. 0= Includes materials that are normally stable, even under fire exposure conditions, and that do not react with water. Normal fire fighting procedures may be used.
[National Fire Protection Guide. Fire Protection Guide on Hazardous Materials. 10 th ed. Quincy, MA: National Fire Protection Association, 1991.,p. 325M-69]**PEER REVIEWED**

Flammable Limits:

LOWER 1.4% @ 93 DEG C (200 DEG F), UPPER 11.4% @ 93 DEG C (200 DEG F)
[National Fire Protection Guide. Fire Protection Guide on Hazardous Materials. 10 th ed. Quincy, MA: National Fire Protection Association, 1991.,p. 325M-69]**PEER REVIEWED**

Flash Point:

-9 deg C (16 deg F) closed cup
[National Fire Protection Guide. Fire Protection Guide on Hazardous Materials. 10 th ed. Quincy, MA: National Fire Protection Association, 1991.,p. 325M-69]**PEER REVIEWED**

22 deg F (Tag open cup)
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 2239]**PEER REVIEWED**

Autoignition Temperature:

404 deg C (759 deg F)
[National Fire Protection Guide. Fire Protection Guide on Hazardous Materials. 10 th ed. Quincy, MA: National Fire Protection Association, 1991.,p. 325M-69]**PEER REVIEWED**

Fire Fighting Procedures:

ALC FOAM, DRY CHEMICAL, OR CARBON DIOXIDE
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

If material on fire or involved in fire: Do not extinguish fire unless flow can be stopped or safely confined. Use water in flooding quantities as fog. Solid streams of water may be ineffective. Cool all affected containers with flooding quantities of water. Apply water from as far a distance as possible. Use alcohol foam, dry chemical or carbon dioxide.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 704]**PEER REVIEWED**

Flammable. Flashback along vapor trail may occur. Vapor may explode if ignited in an enclosed area. Extinguish with dry chemical, alcohol foam, or carbon dioxide. Water may be ineffective on fire. Cool exposed containers with water.
[Prager, J.C. Environmental Contaminant Reference Databook Volume 1. New York, NY: Van Nostrand Reinhold, 1995. 350]**PEER REVIEWED**

Firefighting Hazards:

Flashback along vapor trail may occur.
[Prager, J.C. Environmental Contaminant Reference Databook Volume 1. New York, NY: Van Nostrand Reinhold, 1995. 350]**PEER REVIEWED**

Explosive Limits & Potential:

UPPER 10%; LOWER 1.8%
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 1171]**PEER REVIEWED**

Hazardous Reactivities & Incompatibilities:

Avoid copper
[DLA/DOD; Hazardous Materials Info System #6810-00-N00-0021 (1982)]**PEER REVIEWED**

Incompatible with chloroform, hydrogen peroxide, nitric acid, potassium t-butoxide, and 2-propanol.
[Bretherick, L. Handbook of Reactive Chemical Hazards. 4th ed. Boston, MA: Butterworth-Heinemann Ltd., 1990 465]**PEER REVIEWED**

MIXING **METHYL ETHYL KETONE** & CHLOROSULFONIC ACID OR OLEUM IN A CLOSED CONTAINER CAUSED THE TEMP & PRESSURE TO INCR.
[McEvoy G.K. (ed.). American Hospital Formulary Service-Drug Information 96. Bethesda, MD: American Society of Health-System Pharmacists, Inc. 1996 (Plus Supplements).,p. 491M-90]**PEER REVIEWED**

Strong oxidizers, amines, ammonia, inorganic acids, caustics, copper, isocyanates, pyridines.

[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 36]**QC REVIEWED**

Reaction with hydrogen peroxide + nitric acid forms a heat- and shock-sensitive explosive product. Ignition on contact with potassium t-butoxide. Mixture with 2-propanol will produce explosive peroxides during storage. Vigorous reaction with chloroform + alkali. Incompatible with chlorosulfonic acid; oleum.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 2239]**PEER REVIEWED**

Hazardous Decomposition:

MEK in air is rapidly decomposed by photochemical processes, mainly through oxidation by hydroxyl free radicals as well as some decomposition by direct photolysis ... /with a/ half-life of 5.4 hr for photochemical decomposition in urban atmospheres.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.36 (1993)]**PEER REVIEWED**

When heated to decomposition it emits acrid smoke and fumes.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 2239]**PEER REVIEWED**

Immediately Dangerous to Life or Health:

3000 ppm
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 36]**QC REVIEWED**

Protective Equipment & Clothing:

ORG CANISTER OR AIR PACK; PLASTIC GLOVES
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Skin contact should be avoided by the use of protective gloves; goggles may also be necessary to prevent eye contact. /Ketones/
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 1173]**PEER REVIEWED**

Breakthrough times greater than one hour reported by (normally) two or more testers were found for butyl rubber gloves.
[ACGIH; Guidelines Select of Chem Protect Clothing Volume #1 Field Guide p.68 (1983)]**PEER REVIEWED**

Breakthrough times less (usually significantly less) than one hour reported by (normally) two or more testers were found for natural rubber latex gloves, unsupported; neoprene/natural rubber blend; nitrile rubber glove, unsupported; polyethylene glove; polyvinyl alcohol glove, supported; polyvinyl chloride glove, unsupported; and viton, raw material.
[ACGIH; Guidelines Select of Chem Protect Clothing Volume #1 Field Guide p.68 (1983)]**PEER REVIEWED**

Wear appropriate personal protective clothing to prevent skin contact.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 36]**QC REVIEWED**

Wear appropriate eye protection to prevent eye contact.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 36]**QC REVIEWED**

Eyewash fountains should be provided in areas where there is any possbility that workers could be exposed to the substance; this is irrespective of the recommendation involving the wearing of eye protection.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 36]**QC REVIEWED**

Recommendations for respirator selection. Max concn for use: 3000 ppm. Respirator Class(es): Any supplied-air respirator operated in a continuous flow mode. eye protection needed. Any powered, air-purifying respirator with organic vapor cartridge(s). Eye protection needed. Any chemical cartridge respirator with a full facepiece and organic vapor cartridge(s). Any air-purifying, full-facepiece respirator (gas mask) with a chin-style, front- or back-mounted organic vapor canister. Any self-contained breathing apparatus with a full facepiece. Any supplied-air respirator with a full facepiece.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 36]**QC REVIEWED**

Recommendations for respirator selection. Condition: Emergency or planned entry into unknown concn or IDLH conditions: Respirator Class(es): Any self-contained breathing apparatus that has a full facepiece and is operated in a pressure-demand or other positive pressure mode. Any supplied-air respirator that has a full face piece and is operated in pressure-demand or other positive pressure mode in combination with an auxiliary self-contained breathing apparatus operated in pressure-demand or other positive pressure mode.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 36]**QC REVIEWED**

Recommendations for respirator selection. Condition: Escape from suddenly occurring respiratory hazards: Respirator Class(es): Any air-purifying, full-facepiece respirator (gas mask) with a chin-style, front- or back-mounted organic vapor canister. Any appropriate escape-type, self-contained breathing apparatus.

[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 36]**QC REVIEWED**

Preventive Measures:

Work practices and industrial hygiene techniques should minimize the volatilization of ketones in the workroom air in order to ensure that the exposure limits are not exceeded. /Ketones/
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 1173]**PEER REVIEWED**

If material not on fire and not involved in fire: Keep sparks, flames, and other sources of ignition away. Keep material out of water sources and sewers. Build dikes to contain flow as necessary. Attempt to stop leak if without hazard. Use water spray to disperse vapors and dilute standing pools of liquid.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 704]**PEER REVIEWED**

Evacuation: If material leaking (not on fire) consider evacuation from downwind area based on amount of material spilled, location and weather conditions.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 704]**PEER REVIEWED**

Personnel protection: Avoid breathing vapors. Keep upwind. ... Do not handle broken packages without protective equipment. Wash away any material which may have contacted the body with copious amounts of water or soap and water.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 704]**PEER REVIEWED**

A major concern in the painting studio is solvents, /including **methyl ethyl ketone/. ...** Precautions include ... use of dilution and local exhaust ventilation, control of storage areas, disposal of solvent soaked rags in covered containers, minimizing skin exposure and the use of respirators and other personal protective equipment. The control of fire hazards is also important, since many of the solvents are highly flammable.
[Hart C; J Environ Health 49 (5): 282-6 (1987)]**PEER REVIEWED**

SRP: Local exhaust ventilation should be applied wherever there is an incidence of point source emissions or dispersion of regulated contaminants in the work area. Ventilation control of the contaminant as close to its point of generation is both the most economical and safest method to minimize personnel exposure to airborne contaminants.
PEER REVIEWED

Contact lenses should not be worn when working with this chemical.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 36]**QC REVIEWED**

SRP: The scientific literature for the use of contact lenses in industry is conflicting. The benefit or detrimental effects of wearing contact lenses depend not only upon the substance, but also on factors including the form of the substance, characteristics and duration of the exposure, the uses of other eye protection equipment, and the hygiene of the lenses. However, there may be individual substances whose irritating or corrosive properties are such that the wearing of contact lenses would be harmful to the eye. In those specific cases, contact lenses should not be worn. In any event, the usual eye protection equipment should be worn even when contact lenses are in place.
PEER REVIEWED

SRP: Contaminated protective clothing should be segregated in such a manner so that there is no direct personal contact by personnel who handle, dispose, or clean the clothing. Quality assurance to ascertain the completeness of the cleaning procedures should be implemented before the decontaminated protective clothing is returned for reuse by the workers.
PEER REVIEWED

The worker should immediately wash the skin when it becomes contaminated.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 36]**QC REVIEWED**

Work clothing that becomes wet should be immediately removed due to its flammability hazard.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 36]**QC REVIEWED**

Stability/Shelf Life:

Stability during transport: stable
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Shipment Methods and Regulations:

No person may /transport,/ offer or accept a hazardous material for transportation in commerce unless that person is registered in conformance ... and the hazardous material is properly classed, described, packaged, marked, labeled, and in condition for shipment as required or authorized by ... /the hazardous materials regulations (49 CFR 171-177)./
[49 CFR 171.2 (7/1/96)]**PEER REVIEWED**

The International Air Transport Association (IATA) Dangerous Goods Regulations are published by the IATA Dangerous Goods Board pursuant to IATA Resolutions 618 and 619 and constitute a manual of industry carrier regulations to be followed by all IATA Member airlines when transporting hazardous materials.
[IATA. Dangerous Goods Regulations. 38th ed. Montreal, Canada and Geneva, Switzerland: International Air Transport Association, Dangerous Goods Board, January, 1997. 179]**PEER REVIEWED**

The International Maritime Dangerous Goods Code lays down basic principles for transporting

hazardous chemicals. Detailed recommendations for individual substances and a number of recommendations for good practice are included in the classes dealing with such substances. A general index of technical names has also been compiled. This index should always be consulted when attempting to locate the appropriate procedures to be used when shipping any substance or article.
[IMDG; International Maritime Dangerous Goods Code; International Maritime Organization p.3080 (1988)]**PEER REVIEWED**

Cleanup Methods:

The Hazardous Materials Technical Center (HMTC), an EPA emergency response cleanup services contractor cleaned up a **methyl ethyl ketone (**MEK) spill and decontaminated the groundwater. The spill cleanup involved removing low concentrations of MEK from groundwater. The spill was caused by an overturned tank truck containing 7200 gallons of MEK. MEK was directed into four dry wells that served as primary storm drainage. Immediately after the incident, 6000 gallons of water were pumped from the dry well; 2400 gallons of MEK were recovered from the water. About 1500 gallons of MEK were removed from the truck, and the remaining 3300 gallons of MEK either vaporized or entered an unsaturated zone. MEK concentrations up to 2200 mg/l were reduced to 50 ug/l before reinjection. Levels of MEK in the sample wells, production wells, and reinjection wells were reduced to nondetectable levels.
[Halvorsen F, Ohneck R; Proceedings of the National Conference on Hazardous Wastes and Environmental Emergencies p.193-95 (1985)]**PEER REVIEWED**

Environmental considerations -- air spill: Apply water spray or mist to knock down vapors.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 704]**PEER REVIEWED**

Environmental considerations -- water spill: Use natural barriers or oil spill control booms to limit spill travel. Remove trapped material with suction hoses.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 704]**PEER REVIEWED**

Environmental considerations -- land spill: Dig a pit, pond, lagoon, holding area to contain liquid or solid material. /SRP: If time permits, pits, ponds, lagoons, soak holes, or holding areas should be sealed with an impermeable flexible membrane liner./ Absorb bulk liquid with fly ash, cement powder, or commercial sorbents.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 704]**PEER REVIEWED**

Disposal Methods:

Generators of waste (equal to or greater than 100 kg/mo) containing this contaminant, EPA hazardous waste number F005, must conform with USEPA regulations in storage, transportation, treatment and disposal of waste.
[40 CFR 240-280, 300-306, 702-799 (7/1/96)]**PEER REVIEWED**

Generators of waste (equal to or greater than 100 kg/mo) containing this contaminant, EPA hazardous waste number U159, must conform with USEPA regulations in storage, transportation, treatment and disposal of waste.
[40 CFR 240-280, 300-306, 702-799 (7/1/96)]**PEER REVIEWED**

Incineration. Recommendable methods: Incineration, open burning, use as a fuel, evaporation, discharge to sewer. Peer-review: Potentially contains peroxides which may be explosive. Evaporate small amt only. (Peer-review conclusions of an IRPTC expert consultation (May 1985))
[United Nations. Treatment and Disposal Methods for Waste Chemicals (IRPTC File). Data Profile Series No. 5. Geneva, Switzerland: United Nations Environmental Programme, Dec. 1985. 116]**PEER REVIEWED**

A good candidate for fluidized bed incineration at a temperature range of 450 to 980 deg C and residence times of seconds for liquids and gases, and longer for solids. A good candidate for rotary kiln incineration at a temperature range of 820 to 1,600 deg C and residence times of seconds for liquids and gases, and hours for solids. A good candidate for liquid injection incineration at a temperature range of 650 to 1,600 deg C and a residence time of 0.1 to 2 seconds.
[USEPA; Engineering Handbook for Hazardous Waste Incineration p.3-14 (1981) EPA 68-03-3025]**PEER REVIEWED**

The following wastewater treatment technologies have been investigated for **methyl ethyl ketone:** solvent extraction and activated carbon.
[USEPA; Management of Hazardous Waste Leachate, EPA Contract No.68-03-2766 p.E-16 (1982)]**PEER REVIEWED**

Methyl ethyl ketone is a waste chemical stream constituent which may be subjected to ultimate disposal by controlled incineration.
[USEPA; Engineering Handbook for Hazardous Waste Incineration p.2-8 (1981) EPA 68-03-3025]**PEER REVIEWED**

Spray into incinerator or burn in paper packaging. More flammable solvent may be added.
[Prager, J.C. Environmental Contaminant Reference Databook Volume 1. New York, NY: Van Nostrand Reinhold, 1995. 349]**PEER REVIEWED**

METHYL ETHYL KETONE

CASRN: 78-93-3

For other data, click on the Table of Contents

DOT Emergency Guidelines:

Fire or explosion: HIGHLY FLAMMABLE: Will be easily ignited by heat, sparks or flames. Vapors may form explosive mixtures with air. Vapors may travel to source of ignition and flash back. Most vapors are heavier than air. They will spread along ground and collect in low or confined areas (sewers, basements, tanks). Vapor explosion hazard indoors, outdoors or in sewers. Some may polymerize (P) explosively when heated or involved in a fire. Runoff to sewer may create fire or explosion hazard. Containers may explode when heated. Many liquids are lighter than water.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-127]**PEER REVIEWED**

Health: Inhalation or contact with material may irritate or burn skin and eyes. Fire may produce irritating, corrosive and/or toxic gases. Vapors may cause dizziness or suffocation. Runoff from fire control may cause pollution.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-127]**PEER REVIEWED**

Public safety: CALL Emergency Response Telephone Number. ... Isolate spill or leak area immediately for at least 25 to 50 meters (80 to 160 feet) in all directions. Keep unauthorized personnel away. Stay upwind. Keep out of low areas. Ventilate closed spaces before entering.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-127]**PEER REVIEWED**

Protective clothing: Wear positive pressure self-contained breathing apparatus (SCBA). Structural firefighters' protective clothing will only provide limited protection.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-127]**PEER REVIEWED**

Evacuation: Large spill: Consider initial downwind evacuation for at least 300 meters (1000 feet). Fire: If tank, rail car or tank truck is involved in a fire, ISOLATE for 800 meters (1/2 mile) in all directions; also, consider initial evacuation for 800 meters (1/2 mile) in all directions.
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Fire: CAUTION: All these products have a very low flash point: Use of water spray when fighting fire may be inefficient. Small fires: Dry chemical, CO2, water spray or alcohol-resistant foam. Large fires: Water spray, fog or alcohol-resistant foam. Do not use straight streams. Move containers from fire area if you can do it without risk. Fire involving tanks or car/trailer loads: Fight fire from maximum distance or use unmanned hose holders or monitor nozzles. Cool containers with flooding quantities of water until well after fire is out. Withdraw immediately in case of rising sound from venting safety devices or discoloration of tank. ALWAYS stay away from the ends of tanks. For massive fire, use unmanned hose holders or monitor nozzles; if this is impossible, withdraw from area and let fire burn.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-127]**PEER REVIEWED**

Spill or leak: ELIMINATE all ignition sources (no smoking, flares, sparks or flames in immediate area). All equipment used when handling the product must be grounded. Do not touch or walk through spilled material. Stop leak if you can do it without risk. Prevent entry into waterways, sewers, basements or confined areas. A vapor suppressing foam may be used to reduce vapors. Absorb or cover with dry earth, sand or other non-combustible material and transfer to containers. Use clean non-sparking tools to collect absorbed material. Large spills: Dike far ahead of liquid spill for later disposal. Water spray may reduce vapor; but may not prevent ignition in closed spaces.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-127]**PEER REVIEWED**

First aid: Move victim to fresh air. Call emergency medical care. Apply artificial respiration if victim is not breathing. Administer oxygen if breathing is difficult. Remove and isolate contaminated clothing and shoes. In case of contact with substance, immediately flush skin or eyes with running water for at least 20 minutes. Wash skin with soap and water. Keep victim warm and quiet. Ensure that medical personnel are aware of the material(s) involved, and take precautions to protect themselves.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S.

Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-127]**PEER REVIEWED**

METHYL ETHYL KETONE

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For other data, click on the Table of Contents

Odor Threshold:

Odor low= 0.7375 mg/cu m; Odor high= 147.5 mg/cu m.
[Ruth JH; Am Ind Hyg Assoc J 47: A-142-51 (1986)]**PEER REVIEWED**

Detection limit in water: 5.00x10+1 ppm (purity not specified)
[Fazzalari, F.A. (ed.). Compilation of Odor and Taste Threshold Values Data. ASTM Data Series DS 48A (Committee E-18). Philadelphia, PA: American Society for Testing and Materials, 1978. 24]**PEER REVIEWED**

Recognition in air: 1.00x10+1 ppm (chemically pure)
[Fazzalari, F.A. (ed.). Compilation of Odor and Taste Threshold Values Data. ASTM Data Series DS 48A (Committee E-18). Philadelphia, PA: American Society for Testing and Materials, 1978. 24]**PEER REVIEWED**

Detection limit in air: 2.00x10+1 ppm (purity not specified)
[Fazzalari, F.A. (ed.). Compilation of Odor and Taste Threshold Values Data. ASTM Data Series DS 48A (Committee E-18). Philadelphia, PA: American Society for Testing and Materials, 1978. 24]**PEER REVIEWED**

Recognition in air: 5.50x10+1 ppm (purity not specified)
[Fazzalari, F.A. (ed.). Compilation of Odor and Taste Threshold Values Data. ASTM Data Series DS 48A (Committee E-18). Philadelphia, PA: American Society for Testing and Materials, 1978. 24]**PEER REVIEWED**

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Fire Potential:

Highly flammable liquid.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 2239]**PEER REVIEWED**

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NFPA Hazard Classification:

Health: 1. 1= Materials that, on exposure, would cause irritation, but only minor residual injury, including those requiring the use of an approved air-purifying respirator. These materials are only slightly hazardous to health and breathing protection is needed.
[National Fire Protection Guide. Fire Protection Guide on Hazardous Materials. 10 th ed. Quincy, MA: National Fire Protection Association, 1991.,p. 325M-69]**PEER REVIEWED**

Flammability: 3. 3= Includes Class IB and IC flammable liquids and materials that can be easily ignited under almost all normal temp conditions. Water may be ineffective in controlling or extinguishing fires in such materials.
[National Fire Protection Guide. Fire Protection Guide on Hazardous Materials. 10 th ed. Quincy, MA: National Fire Protection Association, 1991.,p. 325M-69]**PEER REVIEWED**

Reactivity: 0. 0= Includes materials that are normally stable, even under fire exposure conditions, and that do not react with water. Normal fire fighting procedures may be used.
[National Fire Protection Guide. Fire Protection Guide on Hazardous Materials. 10 th ed. Quincy, MA: National Fire Protection Association, 1991.,p. 325M-69]**PEER REVIEWED**

METHYL ETHYL KETONE

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For other data, click on the Table of Contents

Flammable Limits:

LOWER 1.4% @ 93 DEG C (200 DEG F), UPPER 11.4% @ 93 DEG C (200 DEG F)
[National Fire Protection Guide. Fire Protection Guide on Hazardous Materials. 10 th ed. Quincy, MA: National Fire Protection Association, 1991.,p. 325M-69]**PEER REVIEWED**

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For other data, click on the Table of Contents

Flash Point:

-9 deg C (16 deg F) closed cup

[National Fire Protection Guide. Fire Protection Guide on Hazardous Materials. 10 th ed. Quincy, MA: National Fire Protection Association, 1991.,p. 325M-69]**PEER REVIEWED**

22 deg F (Tag open cup)

[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 2239]**PEER REVIEWED**

METHYL ETHYL KETONE

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For other data, click on the Table of Contents

Autoignition Temperature:

404 deg C (759 deg F)

[National Fire Protection Guide. Fire Protection Guide on Hazardous Materials. 10 th ed. Quincy, MA: National Fire Protection Association, 1991.,p. 325M-69]**PEER REVIEWED**

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For other data, click on the Table of Contents

Fire Fighting Procedures:

ALC FOAM, DRY CHEMICAL, OR CARBON DIOXIDE

[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

If material on fire or involved in fire: Do not extinguish fire unless flow can be stopped or safely confined. Use water in flooding quantities as fog. Solid streams of water may be ineffective. Cool all affected containers with flooding quantities of water. Apply water from as far a distance as possible. Use alcohol foam, dry chemical or carbon dioxide.

[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 704]**PEER REVIEWED**

Flammable. Flashback along vapor trail may occur. Vapor may explode if ignited in an enclosed area. Extinguish with dry chemical, alcohol foam, or carbon dioxide. Water may be ineffective on fire. Cool exposed containers with water.

[Prager, J.C. Environmental Contaminant Reference Databook Volume 1. New York, NY: Van Nostrand Reinhold, 1995. 350]**PEER REVIEWED**

METHYL ETHYL KETONE

CASRN: 78-93-3

For other data, click on the Table of Contents

Firefighting Hazards:

Flashback along vapor trail may occur.

[Prager, J.C. Environmental Contaminant Reference Databook Volume 1. New York, NY: Van Nostrand Reinhold, 1995. 350]**PEER REVIEWED**

METHYL ETHYL KETONE

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For other data, click on the Table of Contents

Explosive Limits & Potential:

UPPER 10%; LOWER 1.8%

[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 1171]**PEER REVIEWED**

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Hazardous Reactivities & Incompatibilities:

Avoid copper

[DLA/DOD; Hazardous Materials Info System #6810-00-N00-0021 (1982)]**PEER REVIEWED**

Incompatible with chloroform, hydrogen peroxide, nitric acid, potassium t-butoxide, and 2-propanol.

[Bretherick, L. Handbook of Reactive Chemical Hazards. 4th ed. Boston, MA: Butterworth-Heinemann Ltd., 1990 465]**PEER REVIEWED**

MIXING **METHYL ETHYL KETONE** & CHLOROSULFONIC ACID OR OLEUM IN A CLOSED CONTAINER CAUSED THE TEMP & PRESSURE TO INCR.

[McEvoy G.K. (ed.). American Hospital Formulary Service-Drug Information 96. Bethesda, MD: American Society of Health-System Pharmacists, Inc. 1996 (Plus Supplements).,p. 491M-90]**PEER REVIEWED**

Strong oxidizers, amines, ammonia, inorganic acids, caustics, copper, isocyanates, pyridines.

[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 36]**QC REVIEWED**

Reaction with hydrogen peroxide + nitric acid forms a heat- and shock-sensitive explosive product. Ignition on contact with potassium t-butoxide. Mixture with 2-propanol will produce explosive peroxides during storage. Vigorous reaction with chloroform + alkali. Incompatible with chlorosulfonic acid; oleum.

[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 2239]**PEER REVIEWED**

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Hazardous Decomposition:

MEK in air is rapidly decomposed by photochemical processes, mainly through oxidation by hydroxyl free radicals as well as some decomposition by direct photolysis ... /with a/ half-life of 5.4 hr for photochemical decomposition in urban atmospheres.
[WHO; Environ Health Criteria 143: Methyl Ethyl Ketone p.36 (1993)]**PEER REVIEWED**

When heated to decomposition it emits acrid smoke and fumes.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 2239]**PEER REVIEWED**

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Immediately Dangerous to Life or Health:

3000 ppm

[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 36]**QC REVIEWED**

METHYL ETHYL KETONE

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Protective Equipment & Clothing:

ORG CANISTER OR AIR PACK; PLASTIC GLOVES

[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Skin contact should be avoided by the use of protective gloves; goggles may also be necessary to prevent eye contact. /Ketones/

[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 1173]**PEER REVIEWED**

Breakthrough times greater than one hour reported by (normally) two or more testers were found for butyl rubber gloves.

[ACGIH; Guidelines Select of Chem Protect Clothing Volume #1 Field Guide p.68 (1983)]**PEER REVIEWED**

Breakthrough times less (usually significantly less) than one hour reported by (normally) two or more testers were found for natural rubber latex gloves, unsupported; neoprene/natural rubber blend; nitrile rubber glove, unsupported; polyethylene glove; polyvinyl alcohol glove, supported; polyvinyl chloride glove, unsupported; and viton, raw material.

[ACGIH; Guidelines Select of Chem Protect Clothing Volume #1 Field Guide p.68 (1983)]**PEER REVIEWED**

Wear appropriate personal protective clothing to prevent skin contact.

[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 36]**QC REVIEWED**

Wear appropriate eye protection to prevent eye contact.

[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 36]**QC REVIEWED**

Eyewash fountains should be provided in areas where there is any possbility that workers could be exposed to the substance; this is irrespective of the recommendation involving the wearing of eye protection.

[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 36]**QC REVIEWED**

Recommendations for respirator selection. Max concn for use: 3000 ppm. Respirator Class(es): Any supplied-air respirator operated in a continuous flow mode. eye protection needed. Any powered, air-purifying respirator with organic vapor cartridge(s). Eye protection needed. Any chemical cartridge

respirator with a full facepiece and organic vapor cartridge(s). Any air-purifying, full-facepiece respirator (gas mask) with a chin-style, front- or back-mounted organic vapor canister. Any self-contained breathing apparatus with a full facepiece. Any supplied-air respirator with a full facepiece.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 36]**QC REVIEWED**

Recommendations for respirator selection. Condition: Emergency or planned entry into unknown concn or IDLH conditions: Respirator Class(es): Any self-contained breathing apparatus that has a full facepiece and is operated in a pressure-demand or other positive pressure mode. Any supplied-air respirator that has a full face piece and is operated in pressure-demand or other positive pressure mode in combination with an auxiliary self-contained breathing apparatus operated in pressure-demand or other positive pressure mode.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 36]**QC REVIEWED**

Recommendations for respirator selection. Condition: Escape from suddenly occurring respiratory hazards: Respirator Class(es): Any air-purifying, full-facepiece respirator (gas mask) with a chin-style, front- or back-mounted organic vapor canister. Any appropriate escape-type, self-contained breathing apparatus.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 36]**QC REVIEWED**

METHYL ETHYL KETONE

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For other data, click on the Table of Contents

Preventive Measures:

Work practices and industrial hygiene techniques should minimize the volatilization of ketones in the workroom air in order to ensure that the exposure limits are not exceeded. /Ketones/
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 1173]**PEER REVIEWED**

If material not on fire and not involved in fire: Keep sparks, flames, and other sources of ignition away. Keep material out of water sources and sewers. Build dikes to contain flow as necessary. Attempt to stop leak if without hazard. Use water spray to disperse vapors and dilute standing pools of liquid.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 704]**PEER REVIEWED**

Evacuation: If material leaking (not on fire) consider evacuation from downwind area based on amount of material spilled, location and weather conditions.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 704]**PEER REVIEWED**

Personnel protection: Avoid breathing vapors. Keep upwind. ... Do not handle broken packages without protective equipment. Wash away any material which may have contacted the body with copious amounts of water or soap and water.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 704]**PEER REVIEWED**

A major concern in the painting studio is solvents, /including **methyl ethyl ketone/. ...** Precautions include ... use of dilution and local exhaust ventilation, control of storage areas, disposal of solvent soaked rags in covered containers, minimizing skin exposure and the use of respirators and other personal protective equipment. The control of fire hazards is also important, since many of the solvents are highly flammable.
[Hart C; J Environ Health 49 (5): 282-6 (1987)]**PEER REVIEWED**

SRP: Local exhaust ventilation should be applied wherever there is an incidence of point source emissions or dispersion of regulated contaminants in the work area. Ventilation control of the contaminant as close to its point of generation is both the most economical and safest method to minimize personnel exposure to airborne contaminants.
PEER REVIEWED

Contact lenses should not be worn when working with this chemical.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing

Office, 1997. 36]**QC REVIEWED**

SRP: The scientific literature for the use of contact lenses in industry is conflicting. The benefit or detrimental effects of wearing contact lenses depend not only upon the substance, but also on factors including the form of the substance, characteristics and duration of the exposure, the uses of other eye protection equipment, and the hygiene of the lenses. However, there may be individual substances whose irritating or corrosive properties are such that the wearing of contact lenses would be harmful to the eye. In those specific cases, contact lenses should not be worn. In any event, the usual eye protection equipment should be worn even when contact lenses are in place.
PEER REVIEWED

SRP: Contaminated protective clothing should be segregated in such a manner so that there is no direct personal contact by personnel who handle, dispose, or clean the clothing. Quality assurance to ascertain the completeness of the cleaning procedures should be implemented before the decontaminated protective clothing is returned for reuse by the workers.
PEER REVIEWED

The worker should immediately wash the skin when it becomes contaminated.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 36]**QC REVIEWED**

Work clothing that becomes wet should be immediately removed due to its flammability hazard.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 36]**QC REVIEWED**

METHYL ETHYL KETONE

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For other data, click on the Table of Contents

Stability/Shelf Life:

Stability during transport: stable

[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

METHYL ETHYL KETONE

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For other data, click on the Table of Contents

Shipment Methods and Regulations:

No person may /transport,/ offer or accept a hazardous material for transportation in commerce unless that person is registered in conformance ... and the hazardous material is properly classed, described, packaged, marked, labeled, and in condition for shipment as required or authorized by ... /the hazardous materials regulations (49 CFR 171-177)./

[49 CFR 171.2 (7/1/96)]**PEER REVIEWED**

The International Air Transport Association (IATA) Dangerous Goods Regulations are published by the IATA Dangerous Goods Board pursuant to IATA Resolutions 618 and 619 and constitute a manual of industry carrier regulations to be followed by all IATA Member airlines when transporting hazardous materials.

[IATA. Dangerous Goods Regulations. 38th ed. Montreal, Canada and Geneva, Switzerland: International Air Transport Association, Dangerous Goods Board, January, 1997. 179]**PEER REVIEWED**

The International Maritime Dangerous Goods Code lays down basic principles for transporting hazardous chemicals. Detailed recommendations for individual substances and a number of recommendations for good practice are included in the classes dealing with such substances. A general index of technical names has also been compiled. This index should always be consulted when attempting to locate the appropriate procedures to be used when shipping any substance or article.

[IMDG; International Maritime Dangerous Goods Code; International Maritime Organization p.3080 (1988)]**PEER REVIEWED**

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Cleanup Methods:

The Hazardous Materials Technical Center (HMTC), an EPA emergency response cleanup services contractor cleaned up a **methyl ethyl ketone (**MEK) spill and decontaminated the groundwater. The spill cleanup involved removing low concentrations of MEK from groundwater. The spill was caused by an overturned tank truck containing 7200 gallons of MEK. MEK was directed into four dry wells that served as primary storm drainage. Immediately after the incident, 6000 gallons of water were pumped from the dry well; 2400 gallons of MEK were recovered from the water. About 1500 gallons of MEK were removed from the truck, and the remaining 3300 gallons of MEK either vaporized or entered an unsaturated zone. MEK concentrations up to 2200 mg/l were reduced to 50 ug/l before reinjection. Levels of MEK in the sample wells, production wells, and reinjection wells were reduced to nondetectable levels.
[Halvorsen F, Ohneck R; Proceedings of the National Conference on Hazardous Wastes and Environmental Emergencies p.193-95 (1985)]**PEER REVIEWED**

Environmental considerations -- air spill: Apply water spray or mist to knock down vapors.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 704]**PEER REVIEWED**

Environmental considerations -- water spill: Use natural barriers or oil spill control booms to limit spill travel. Remove trapped material with suction hoses.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 704]**PEER REVIEWED**

Environmental considerations -- land spill: Dig a pit, pond, lagoon, holding area to contain liquid or solid material. /SRP: If time permits, pits, ponds, lagoons, soak holes, or holding areas should be sealed with an impermeable flexible membrane liner./ Absorb bulk liquid with fly ash, cement powder, or commercial sorbents.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 704]**PEER REVIEWED**

METHYL ETHYL KETONE

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Disposal Methods:

Generators of waste (equal to or greater than 100 kg/mo) containing this contaminant, EPA hazardous waste number F005, must conform with USEPA regulations in storage, transportation, treatment and disposal of waste.
[40 CFR 240-280, 300-306, 702-799 (7/1/96)]**PEER REVIEWED**

Generators of waste (equal to or greater than 100 kg/mo) containing this contaminant, EPA hazardous waste number U159, must conform with USEPA regulations in storage, transportation, treatment and disposal of waste.
[40 CFR 240-280, 300-306, 702-799 (7/1/96)]**PEER REVIEWED**

Incineration. Recommendable methods: Incineration, open burning, use as a fuel, evaporation, discharge to sewer. Peer-review: Potentially contains peroxides which may be explosive. Evaporate small amt only. (Peer-review conclusions of an IRPTC expert consultation (May 1985))
[United Nations. Treatment and Disposal Methods for Waste Chemicals (IRPTC File). Data Profile Series No. 5. Geneva, Switzerland: United Nations Environmental Programme, Dec. 1985. 116]**PEER REVIEWED**

A good candidate for fluidized bed incineration at a temperature range of 450 to 980 deg C and residence times of seconds for liquids and gases, and longer for solids. A good candidate for rotary kiln incineration at a temperature range of 820 to 1,600 deg C and residence times of seconds for liquids and gases, and hours for solids. A good candidate for liquid injection incineration at a temperature range of 650 to 1,600 deg C and a residence time of 0.1 to 2 seconds.
[USEPA; Engineering Handbook for Hazardous Waste Incineration p.3-14 (1981) EPA 68-03-3025]**PEER REVIEWED**

The following wastewater treatment technologies have been investigated for **methyl ethyl ketone:** solvent extraction and activated carbon.
[USEPA; Management of Hazardous Waste Leachate, EPA Contract No.68-03-2766 p.E-16 (1982)]**PEER REVIEWED**

Methyl ethyl ketone is a waste chemical stream constituent which may be subjected to ultimate disposal by controlled incineration.
[USEPA; Engineering Handbook for Hazardous Waste Incineration p.2-8 (1981) EPA 68-03-3025]**PEER REVIEWED**

Spray into incinerator or burn in paper packaging. More flammable solvent may be added.
[Prager, J.C. Environmental Contaminant Reference Databook Volume 1. New York, NY: Van Nostrand Reinhold, 1995. 349]**PEER REVIEWED**

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Occupational Exposure Standards:

OSHA Standards:

Permissible Exposure Limit: Table Z-1 8-hr Time Weighted Avg: 200 ppm (590 mg/cu m).
[29 CFR 1910.1000 (7/1/98)]**QC REVIEWED**

Vacated 1989 OSHA PEL TWA 200 ppm (590 mg/cu m); STEL 300 ppm (885 mg/cu m) is still enforced in some states.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 360]**QC REVIEWED**

Threshold Limit Values:

8 hr Time Weighted Avg (TWA) 200 ppm; Short Term Exposure Limit (STEL) 300 ppm
[American Conference of Governmental Industrial Hygienists. Threshold Limit Values (TLVs) for Chemical Substances and Physical Agents Biological Exposure Indices for 1998. Cincinnati, OH: ACGIH, 1998. 49]**QC REVIEWED**

BEI (Biological Exposure Index): **Methyl ethyl ketone** in urine at end of shift is 2 mg/l. (1988 adoption)
[American Conference of Governmental Industrial Hygienists. Threshold Limit Values (TLVs) for Chemical Substances and Physical Agents Biological Exposure Indices for 1998. Cincinnati, OH: ACGIH, 1998. 102]**QC REVIEWED**

NIOSH Recommendations:

Recommended Exposure Limit: 10 Hr Time-Weighted Avg: 200 ppm (590 mg/cu m).
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 36]**QC REVIEWED**

Recommended Exposure Limit: 15 Min Short-Term Exposure Limit: 300 ppm (885 mg/cu m).
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 36]**QC REVIEWED**

Immediately Dangerous to Life or Health:

3000 ppm
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 36]**QC REVIEWED**

METHYL ETHYL KETONE

CASRN: 78-93-3

For other data, click on the Table of Contents

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Permissible Exposure Limit: Table Z-1 8-hr Time Weighted Avg: 200 ppm (590 mg/cu m).
[29 CFR 1910.1000 (7/1/98)]**QC REVIEWED**

Vacated 1989 OSHA PEL TWA 200 ppm (590 mg/cu m); STEL 300 ppm (885 mg/cu m) is still enforced in some states.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 360]**QC REVIEWED**

METHYL ETHYL KETONE

CASRN: 78-93-3

For other data, click on the Table of Contents

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8 hr Time Weighted Avg (TWA) 200 ppm; Short Term Exposure Limit (STEL) 300 ppm
[American Conference of Governmental Industrial Hygienists. Threshold Limit Values (TLVs) for Chemical Substances and Physical Agents Biological Exposure Indices for 1998. Cincinnati, OH: ACGIH, 1998. 49]**QC REVIEWED**

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[American Conference of Governmental Industrial Hygienists. Threshold Limit Values (TLVs) for Chemical Substances and Physical Agents Biological Exposure Indices for 1998. Cincinnati, OH: ACGIH, 1998. 102]**QC REVIEWED**

METHYL ETHYL KETONE

CASRN: 78-93-3

For other data, click on the Table of Contents

NIOSH Recommendations:

Recommended Exposure Limit: 10 Hr Time-Weighted Avg: 200 ppm (590 mg/cu m).
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 36]**QC REVIEWED**

Recommended Exposure Limit: 15 Min Short-Term Exposure Limit: 300 ppm (885 mg/cu m).
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 36]**QC REVIEWED**

METHYL ETHYL KETONE

CASRN: 78-93-3

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Manufacturing/Use Information:

Major Uses:

AS SOLVENT; IN THE SURFACE COATING INDUSTRY; MFR OF COLORLESS SYNTHETIC RESINS, SMOKELESS POWDER
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 1037]**PEER REVIEWED**

IN FABRIC COATING; IN ARTIFICIAL LEATHER MFR; IN LACQUER & VARNISH INDUSTRY; IN PHARMACEUTICALS & COSMETICS; IN SYNTHETIC RUBBER MFR; IN PRODUCTION OF LUBRICATING OILS
[Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965. 422]**PEER REVIEWED**

PAINT REMOVERS; CEMENTS & ADHESIVES; ORG SYNTHESIS; IN CLEANING FLUIDS
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 12th ed. New York, NY: Van Nostrand Rheinhold Co., 1993 768]**PEER REVIEWED**

SOLVENT FOR COATINGS-ESP VINYL, NITROCELLULOSE & ACRYLIC
[SRI]**PEER REVIEWED**

SOLVENT FOR ADHESIVES & MAGNETIC TAPES
[SRI]**PEER REVIEWED**

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[SRI]**PEER REVIEWED**

SOLVENT FOR PRINTING INKS & IN CLEANING SOLNS
[SRI]**PEER REVIEWED**

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[SRI]**PEER REVIEWED**

OXIDN PROMOTER IN MFR OF TEREPHTHALIC ACID FROM P-XYLENE
[SRI]**PEER REVIEWED**

SOLVENT & COSOLVENT IN PESTICIDE FORMULATIONS
[SRI]**PEER REVIEWED**

FRAGRANCE & FLAVORING AGENT-EG, FOR CANDY & IN PERFUMES (FORMER USES)
[SRI]**PEER REVIEWED**

CATALYST IN THE PRODN OF HYDRAZINE (NON-USA USE)

[SRI]**PEER REVIEWED**

Used as a sterilizer for bacterial spores on surgical instruments, hypodermic needles/syringe, and dental instruments.
[Purdue University; National Pesticide Information Retrieval System (1988)]**PEER REVIEWED**

... Solvent ... required for the polymerization processing of polystyrene, acrylonitrile-butadiene-styrene, and styrene-butadiene-rubber.
[Fishbein L; Industrial Hazards of Plastics and Synthetic Elastomers p.239-62 (1984)]**PEER REVIEWED**

Manufacturers:

Exxon Corp, Hq, 1251 Ave of the Americas, New York, NY 10020, (212) 333-1000; Exxon Chemical Co, division, Exxon Chemical Americas, PO Box 3272, Houston, TX 77001; Production site: Baton Rouge, LA 70821
[SRI. 1996 Directory of Chemical Producers-United States of America. Menlo Park, CA: SRI International, 1996. 744]**PEER REVIEWED**

Hoechst Celanese Corp, Hq, Route 202-206 N, Somerville, NJ 08876, (201) 231-2000; Hoechst Celanese Chemical Group, Inc, 1250 Mockingbird Lane, Dallas, TX 75356-9320; Production site: Pampa, TX 79065
[SRI. 1996 Directory of Chemical Producers-United States of America. Menlo Park, CA: SRI International, 1996. 744]**PEER REVIEWED**

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[SRI]**PEER REVIEWED**

Formulations/Preparations:

GRADES OF PURITY: 99.5+%
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

GRADE: TECHNICAL
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 12th ed. New York, NY: Van Nostrand Rheinhold Co., 1993 768]**PEER REVIEWED**

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SOLVENT FOR VINYL COATINGS, 30%; SOLVENT FOR ADHESIVES, 18%; SOLVENT FOR NITROCELLULOSE COATINGS, 13%; SOLVENT FOR ACRYLIC COATINGS, 11%; SOLVENT FOR OTHER COATINGS, 7%; SOLVENT FOR MAGNETIC TAPES, 7%; EXTRACTION SOLVENT FOR LUBE OIL DEWAXING, 5%; SOLVENT FOR PRINTING INKS, 5%; OTHER, 4% (1981)
[SRI]**PEER REVIEWED**

Projected growth figure through 1983 is 4%. Production of industrial coatings was 3.8% higher in 1978 than year before. Paint and varnish sales grew 13.6% during the same period.
[Kavaler. Chem Market Reporter 1980]**PEER REVIEWED**

CHEMICAL PROFILE: **Methyl Ethyl Ketone.** Coatings solvent, 50%; adhesives, 13%; magnetic tapes, 8%; lube oil dewaxing, 4%; printing inks, 3%; miscellaneous, 6%; exports, 16%.
[Kavaler AR; Chemical Marketing Reporter 232 (8): 50 (1987)]**PEER REVIEWED**

CHEMICAL PROFILE: **Methyl ethyl ketone.** Demand: 1986: 582 million lb; 1987: 600 million lb; 1991 /projected/: 600 million lb (Includes exports; in addition, 52 million lb were imported in 1986).
[Kavaler AR; Chemical Marketing Reporter 232 (8): 50 (1987)]**PEER REVIEWED**

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[SRI]**PEER REVIEWED**

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[USITC SYN ORG CHEM-US PROD/SALES 1985 p.125]**PEER REVIEWED**

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The demand for **methyl ethyl ketone** was 3.0X10+11 g in 1978, 3.7X10+11 g in 1979 and projected to be 3.6X10+11 g in 1983 (production plus imports)
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[SRI]**PEER REVIEWED**

(1985) 3.51X10+10 g
[BUREAU OF THE CENSUS US IMPORTS FOR CONSUMPTION AND GENERAL IMPORTS 1985 p.-580]**PEER REVIEWED**

5.20X10+7 lb
[BUREAU OF THE CENSUS. US IMPORTS FOR CONSUMPTION AND GENERAL IMPORTS 1986 P. 1-526]**PEER REVIEWED**

1995 imports amounted to about 24 million pounds.
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Clinical Laboratory Methods:

HEAD SPACE MASS SPECTROMETRIC SCREENING TECHNIQUE FOR VOLATILES IN BLOOD & POST-MORTEM TISSUES (LIVER, BRAIN, LUNG) IS DESCRIBED.
[URICH RW ET AL; J ANAL TOXICOL 1 (5): 195 (1977)]**PEER REVIEWED**

Venous blood sampled after 2 or more hr of exposure. Processed by Gas Chromatography, FID. Range: 0.1 to 8 ug/ml. Precision: 0.095 (1 ug/ml blood).
[U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. V1 8002-1]**PEER REVIEWED**

Methyl ethyl ketone in biofluid samples is analyzed using headspace chromatography with a flame ionization detector. The relative retention time is 0.816 min (relative to n-propanol 1.50 min).
[Sunshine, Irving (ed.) Methodology for Analytical Toxicology. Cleveland: CRC Press, Inc., 1975.,p. VII/7]**PEER REVIEWED**

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[Kezic S, Monster AC; J Chromatogr 428 (2): 275-80 (1988)]**PEER REVIEWED**

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[TYRAS H ET AL; CHEM ANAL (WARSAW) 21 (3): 647 (1976)]**PEER REVIEWED**

GLASS TUBE PACKED WITH ACTIVATED CHARCOAL IS USED TO TAKE AN INTEGRATED SAMPLE. GAS CHROMATOGRAPH EQUIPPED WITH A FLAME IONIZATION DETECTOR.
[WHITE LD ET AL; AM IND HYG ASSOC J 31 (2): 225 (1970)]**PEER REVIEWED**

ANALYTE: **METHYL ETHYL KETONE;** MATRIX: AIR; RANGE: 0.01 MG/SAMPLE; PROCEDURE: ADSORPTION ON CHARCOAL DESORPTION WITH CARBON DISULFIDE, GC;

PRECISION: NOT GIVEN.
[U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. V1 2500-2]**PEER REVIEWED**

EPA Method 1624 - Volatile Organic Compounds By GC/MS: Grab samples in municipal and industrial discharges are collected. If residual chlorine is present, add sodium thiosulfate. Extraction is performed by a purge and trap apparatus. An isotope dilution gas chromatography/mass spectrometry method for the determination of volatile organic compounds in municipal and industrial discharges is described. Unlabeled **methyl ethyl ketone** has a minimum level of 50 ug/l and a mean retention time of 848 sec.
[40 CFR 136 (7/1/88)]**PEER REVIEWED**

EPA Method 8015: Nonhalogenated Volatile Organics. For the analysis of solid waste, a representative sample (solid or liquid) is collected in a standard 40 ml glass screw-cap VOA vial equipped with a Teflon-faced silicone septum. Sample agitation, as well as contamination of the collected sample with air, must be avoided. Two VOA vials are filled per sample location, then placed in separate plastic bags for shipment and storage. Samples can be analyzed by direct injection or purge-and trap gas chromatography. A temperature program is used in the gas chromatograph to separate the organic compounds. Column 1 is an 8 ft by 0.1 in ID stainless steel or glass column packed with 1% SP-1000 on Carbopack-B 60/80 mesh or equivalent. Column 2 is a 6 ft by 0.1 in ID stainless steel or glass column packed with n-octane on Porasil-C 100/120 mesh (Durapak) or equivalent. Detection is achieved by a flame ionization detector (FID). Under the prescribed conditions, **methyl ethyl ketone** can be detected using this method. No statistical analysis was determined; specific method performance information will be provided as it becomes available.
[USEPA/Office of Solid Waste (OSW); Test Methods for Evaluating Solid Waste, Physical/Chemical Methods SW846 Methods (1986)]**PEER REVIEWED**

Sampling Procedures:

PORTABLE IR ANALYZERS MATED WITH MICROCOMPUTER ARE SUITABLE FOR ON-SITE MONITORING OF MIXTURES OF **METHYL ETHYL KETONE.**
[SYRJALA R; IND RES 19 (6): 81 (1977)]**PEER REVIEWED**

Calibrate each personal sampling pump with sampler in line. Break the ends and attach sampler to personal sampling pump with flexible tubing. Sample at flow rate between 0.01 and 0.2 l/min for total sample size of 1.0 to 12 l.
[U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. V1 2500-1]**PEER REVIEWED**

Activated charcoal, Ambersorb XE-348, and Amberlites XAD-2, XAD-4, and XAD-7 were evaluated as

solid adsorbents for work-room air sampling of acetone, **methyl ethyl ketone,** methyl isobutyl ketone, methyl n-butyl ketone, cyclohexanone and isophorone. Activated charcoal had good capacity for the compounds investigated, but most ketones decomposed on this adsorbent during storage. Ambersorb XE-348 also showed good capacity for most of the ketones and decomposition was insignificant. [Levin JO, Carleborg L; Ann Occup Hyg 31 (1): 31-8 (1987)]**PEER REVIEWED**

ANALYTE: 2-**BUTANONE**; MATRIX: AIR; RANGE: 380-1240 MG/CU M; PROCEDURE: ADSORPTION ON CHARCOAL, DESORPTION WITH CARBON DISULFIDE, GC. [U.S. Department of Health, Education Welfare, Public Health Service. Center for Disease Control, National Institute for Occupational Safety Health. NIOSH Manual ofAnalytical Methods. 2nd ed. Volumes 1-7. Washington, DC: U.S. Government Printing Office, 1977-present.,p. V2 S3-1]**PEER REVIEWED**

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Venous blood sampled after 2 or more hr of exposure. Processed by Gas Chromatography, FID. Range: 0.1 to 8 ug/ml. Precision: 0.095 (1 ug/ml blood).
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[WHITE LD ET AL; AM IND HYG ASSOC J 31 (2): 225 (1970)]**PEER REVIEWED**

ANALYTE: **METHYL ETHYL KETONE;** MATRIX: AIR; RANGE: 0.01 MG/SAMPLE; PROCEDURE: ADSORPTION ON CHARCOAL DESORPTION WITH CARBON DISULFIDE, GC; PRECISION: NOT GIVEN.
[U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. V1 2500-2]**PEER REVIEWED**

EPA Method 1624 - Volatile Organic Compounds By GC/MS: Grab samples in municipal and industrial discharges are collected. If residual chlorine is present, add sodium thiosulfate. Extraction is performed by a purge and trap apparatus. An isotope dilution gas chromatography/mass spectrometry method for the determination of volatile organic compounds in municipal and industrial discharges is described. Unlabeled **methyl ethyl ketone** has a minimum level of 50 ug/l and a mean retention time of 848 sec.
[40 CFR 136 (7/1/88)]**PEER REVIEWED**

EPA Method 8015: Nonhalogenated Volatile Organics. For the analysis of solid waste, a representative sample (solid or liquid) is collected in a standard 40 ml glass screw-cap VOA vial equipped with a Teflon-faced silicone septum. Sample agitation, as well as contamination of the collected sample with air, must be avoided. Two VOA vials are filled per sample location, then placed in separate plastic bags for shipment and storage. Samples can be analyzed by direct injection or purge-and trap gas chromatography. A temperature program is used in the gas chromatograph to separate the organic compounds. Column 1 is an 8 ft by 0.1 in ID stainless steel or glass column packed with 1% SP-1000 on Carbopack-B 60/80 mesh or equivalent. Column 2 is a 6 ft by 0.1 in ID stainless steel or glass column packed with n-octane on Porasil-C 100/120 mesh (Durapak) or equivalent. Detection is achieved by a flame ionization detector (FID). Under the prescribed conditions, **methyl ethyl ketone** can be detected using this method. No statistical analysis was determined; specific method performance information will be provided as it becomes available.
[USEPA/Office of Solid Waste (OSW); Test Methods for Evaluating Solid Waste, Physical/Chemical Methods SW846 Methods (1986)]**PEER REVIEWED**

METHYL ETHYL KETONE

CASRN: 78-93-3

For other data, click on the Table of Contents

Sampling Procedures:

PORTABLE IR ANALYZERS MATED WITH MICROCOMPUTER ARE SUITABLE FOR ON-SITE MONITORING OF MIXTURES OF **METHYL ETHYL KETONE.**
[SYRJALA R; IND RES 19 (6): 81 (1977)]**PEER REVIEWED**

Calibrate each personal sampling pump with sampler in line. Break the ends and attach sampler to personal sampling pump with flexible tubing. Sample at flow rate between 0.01 and 0.2 l/min for total sample size of 1.0 to 12 l.
[U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. V1 2500-1]**PEER REVIEWED**

Activated charcoal, Ambersorb XE-348, and Amberlites XAD-2, XAD-4, and XAD-7 were evaluated as solid adsorbents for work-room air sampling of acetone, **methyl ethyl ketone,** methyl isobutyl ketone, methyl n-butyl ketone, cyclohexanone and isophorone. Activated charcoal had good capacity for the compounds investigated, but most ketones decomposed on this adsorbent during storage. Ambersorb XE-348 also showed good capacity for most of the ketones and decomposition was insignificant.
[Levin JO, Carleborg L; Ann Occup Hyg 31 (1): 31-8 (1987)]**PEER REVIEWED**

ANALYTE: 2-**BUTANONE**; MATRIX: AIR; RANGE: 380-1240 MG/CU M; PROCEDURE: ADSORPTION ON CHARCOAL, DESORPTION WITH CARBON DISULFIDE, GC.
[U.S. Department of Health, Education Welfare, Public Health Service. Center for Disease Control, National Institute for Occupational Safety Health. NIOSH Manual ofAnalytical Methods. 2nd ed. Volumes 1-7. Washington, DC: U.S. Government Printing Office, 1977-present.,p. V2 S3-1]**PEER REVIEWED**

METHYL ETHYL KETONE

CASRN: 78-93-3

For other data, click on the Table of Contents

Special References:

Special Reports:

PANSON RD; WINEK CL, CLIN TOXICOL 17 (2): 271 (1980). REVIEW ARTICLE ON HUMAN & ANIMAL TOXICITY & MGMNT.

OPDYKE DL J; FOOD COSMET TOXICOL 15 (6): 627 (1977). TOXICOLOGY, PREPARATION, PHYSICAL PROPERTIES, METABOLISM, PHARMACOLOGY, TERATOGENICITY, USE IN COSMETICS & IN FOODS ARE REVIEWED.

Yang RS H; Residue Rev 97: 121-43 (1986). The toxicology of **methyl ethyl ketone.** A review with many references on the manufacture, uses, and toxicity of **methyl ethyl ketone.**

Arbetarskyddsstyrelsen, Publikationsservice 171 (84): 133 (1985). Scientific basis for Swedish occupational standards.

USEPA; Health and Environmental Effects Profile for **Methyl Ethyl Ketone** p.80 (1988) EPA/600/X-85/363

DHHS/ATSDR; Toxicological Profile for 2-**Butanone** (1992) ATSDR/TP-91/08

WHO; Environmental Health Criteria 143: **Methyl Ethyl Ketone (**1993)

METHYL ETHYL KETONE

CASRN: 78-93-3

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Special Reports:

PANSON RD; WINEK CL, CLIN TOXICOL 17 (2): 271 (1980). REVIEW ARTICLE ON HUMAN & ANIMAL TOXICITY & MGMNT.

OPDYKE DL J; FOOD COSMET TOXICOL 15 (6): 627 (1977). TOXICOLOGY, PREPARATION, PHYSICAL PROPERTIES, METABOLISM, PHARMACOLOGY, TERATOGENICITY, USE IN COSMETICS & IN FOODS ARE REVIEWED.

Yang RS H; Residue Rev 97: 121-43 (1986). The toxicology of **methyl ethyl ketone.** A review with many references on the manufacture, uses, and toxicity of **methyl ethyl ketone.**

Arbetarskyddsstyrelsen, Publikationsservice 171 (84): 133 (1985). Scientific basis for Swedish occupational standards.

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WHO; Environmental Health Criteria 143: **Methyl Ethyl Ketone (**1993)

METHYL ETHYL KETONE

CASRN: 78-93-3

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Synonyms and Identifiers:

Synonyms:

ACETONE, METHYL-
PEER REVIEWED

AETHYLMETHYLKETON (GERMAN)
PEER REVIEWED

BUTANONE
PEER REVIEWED

2-**BUTANONE**
PEER REVIEWED

3-**BUTANONE**
PEER REVIEWED

BUTANONE 2 (FRENCH)
PEER REVIEWED

Caswell No 569
PEER REVIEWED

EPA Pesticide Chemical Code 044103
PEER REVIEWED

Ethylmethylcetone (French)
PEER REVIEWED

ETHYLMETHYLKETON (DUTCH)
PEER REVIEWED

ETHYL METHYL KETONE
PEER REVIEWED

FEMA no 2170
PEER REVIEWED

KETONE, ETHYL METHYL
PEER REVIEWED

Meetco
PEER REVIEWED

MEK

PEER REVIEWED

METHYL ACETONE
PEER REVIEWED

Metiletilcetona (Spanish)
PEER REVIEWED

METILETILCHETONE (ITALIAN)
PEER REVIEWED

METYLOETYLOKETON (POLISH)
PEER REVIEWED

AI3-07540 (USDA)
PEER REVIEWED

Formulations/Preparations:

GRADES OF PURITY: 99.5+%
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

GRADE: TECHNICAL
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 12th ed. New York, NY: Van Nostrand Rheinhold Co., 1993 768]**PEER REVIEWED**

Shipping Name/ Number DOT/UN/NA/IMO:

UN 1193; Ethyl methyl ketone

IMO 3.2; Ethyl methyl ketone

Standard Transportation Number:

49 092 43; **Methyl ethyl ketone**

EPA Hazardous Waste Number:

U159; A toxic waste when a discarded commercial chemical product or manufacturing chemical intermediate or an off-specification commercial chemical product.

F005; A hazardous waste from nonspecific sources when a spent solvent.

RTECS Number:

NIOSH/EL6475000

METHYL ETHYL KETONE

CASRN: 78-93-3

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Synonyms:

ACETONE, METHYL-
PEER REVIEWED

AETHYLMETHYLKETON (GERMAN)
PEER REVIEWED

BUTANONE
PEER REVIEWED

2-**BUTANONE**
PEER REVIEWED

3-**BUTANONE**
PEER REVIEWED

BUTANONE 2 (FRENCH)
PEER REVIEWED

Caswell No 569
PEER REVIEWED

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Ethylmethylcetone (French)
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ETHYL METHYL KETONE
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FEMA no 2170
PEER REVIEWED

KETONE, ETHYL METHYL
PEER REVIEWED

Meetco
PEER REVIEWED

MEK
PEER REVIEWED

METHYL ACETONE

PEER REVIEWED

Metiletilcetona (Spanish)
PEER REVIEWED

METILETILCHETONE (ITALIAN)
PEER REVIEWED

METYLOETYLOKETON (POLISH)
PEER REVIEWED

AI3-07540 (USDA)
PEER REVIEWED

METHYL ETHYL KETONE

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METHYL ETHYL KETONE

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RTECS Number:

NIOSH/EL6475000

METHYL ETHYL KETONE

CASRN: 78-93-3

For other data, click on the Table of Contents

Administrative Information:

Hazardous Substances Databank Number: 99

Last Revision Date: 20000324

Last Review Date: Reviewed by SRP on 9/18/1997

Update History:

Complete Update on 03/24/2000, 1 field added/edited/deleted.
Complete Update on 02/02/2000, 1 field added/edited/deleted.
Complete Update on 11/16/1999, 1 field added/edited/deleted.
Complete Update on 09/21/1999, 1 field added/edited/deleted.
Complete Update on 08/26/1999, 1 field added/edited/deleted.
Complete Update on 07/20/1999, 5 fields added/edited/deleted.
Complete Update on 03/29/1999, 2 fields added/edited/deleted.
Field Update on 03/19/1999, 1 field added/edited/deleted.
Complete Update on 03/01/1999, 1 field added/edited/deleted.
Complete Update on 01/20/1999, 1 field added/edited/deleted.
Complete Update on 11/12/1998, 1 field added/edited/deleted.
Complete Update on 09/11/1998, 1 field added/edited/deleted.
Complete Update on 06/02/1998, 1 field added/edited/deleted.
Complete Update on 02/25/1998, 1 field added/edited/deleted.
Complete Update on 01/26/1998, 82 fields added/edited/deleted.
Field Update on 10/17/1997, 1 field added/edited/deleted.
Field Update on 09/08/1997, 5 fields added/edited/deleted.
Field Update on 08/13/1997, 5 fields added/edited/deleted.
Complete Update on 03/27/1997, 2 fields added/edited/deleted.
Complete Update on 02/24/1997, 1 field added/edited/deleted.
Complete Update on 12/11/1996, 1 field added/edited/deleted.
Complete Update on 06/06/1996, 1 field added/edited/deleted.
Complete Update on 04/09/1996, 8 fields added/edited/deleted.
Field Update on 01/18/1996, 1 field added/edited/deleted.
Complete Update on 11/10/1995, 1 field added/edited/deleted.
Complete Update on 01/23/1995, 1 field added/edited/deleted.
Complete Update on 12/19/1994, 1 field added/edited/deleted.
Complete Update on 11/18/1994, 1 field added/edited/deleted.
Complete Update on 09/16/1994, 1 field added/edited/deleted.
Complete Update on 08/31/1994, 1 field added/edited/deleted.
Complete Update on 07/28/1994, 1 field added/edited/deleted.
Complete Update on 03/25/1994, 1 field added/edited/deleted.
Complete Update on 08/07/1993, 1 field added/edited/deleted.

Complete Update on 08/04/1993, 1 field added/edited/deleted.
Field update on 12/10/1992, 1 field added/edited/deleted.
Complete Update on 11/25/1992, 1 field added/edited/deleted.
Complete Update on 10/07/1992, 1 field added/edited/deleted.
Complete Update on 09/03/1992, 1 field added/edited/deleted.
Complete Update on 04/27/1992, 1 field added/edited/deleted.
Complete Update on 01/23/1992, 1 field added/edited/deleted.
Complete Update on 05/21/1990, 1 field added/edited/deleted.
Complete Update on 04/16/1990, 2 fields added/edited/deleted.
Complete Update on 01/11/1990, 2 fields added/edited/deleted.
Field update on 12/29/1989, 1 field added/edited/deleted.
Complete Update on 07/28/1989, 85 fields added/edited/deleted.
Field Update on 05/05/1989, 1 field added/edited/deleted.
Complete Update on 08/15/1988, 102 fields added/edited/deleted.
Complete Update on 03/31/1986

Record Length: 193690

METHYL ETHYL KETONE

CASRN: 78-93-3

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Hazardous Substances Databank Number: 99

METHYL ETHYL KETONE

CASRN: 78-93-3

For other data, click on the Table of Contents

Last Revision Date: 20000324

METHYL ETHYL KETONE

CASRN: 78-93-3

For other data, click on the Table of Contents

Last Review Date: Reviewed by SRP on 9/18/1997

METHYL ETHYL KETONE

CASRN: 78-93-3

For other data, click on the Table of Contents

Update History:

Complete Update on 03/24/2000, 1 field added/edited/deleted.
Complete Update on 02/02/2000, 1 field added/edited/deleted.
Complete Update on 11/16/1999, 1 field added/edited/deleted.
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Complete Update on 08/26/1999, 1 field added/edited/deleted.
Complete Update on 07/20/1999, 5 fields added/edited/deleted.
Complete Update on 03/29/1999, 2 fields added/edited/deleted.
Field Update on 03/19/1999, 1 field added/edited/deleted.
Complete Update on 03/01/1999, 1 field added/edited/deleted.
Complete Update on 01/20/1999, 1 field added/edited/deleted.
Complete Update on 11/12/1998, 1 field added/edited/deleted.
Complete Update on 09/11/1998, 1 field added/edited/deleted.
Complete Update on 06/02/1998, 1 field added/edited/deleted.
Complete Update on 02/25/1998, 1 field added/edited/deleted.
Complete Update on 01/26/1998, 82 fields added/edited/deleted.
Field Update on 10/17/1997, 1 field added/edited/deleted.
Field Update on 09/08/1997, 5 fields added/edited/deleted.
Field Update on 08/13/1997, 5 fields added/edited/deleted.
Complete Update on 03/27/1997, 2 fields added/edited/deleted.
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Complete Update on 04/09/1996, 8 fields added/edited/deleted.
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Complete Update on 08/04/1993, 1 field added/edited/deleted.
Field update on 12/10/1992, 1 field added/edited/deleted.
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Complete Update on 10/07/1992, 1 field added/edited/deleted.
Complete Update on 09/03/1992, 1 field added/edited/deleted.
Complete Update on 04/27/1992, 1 field added/edited/deleted.
Complete Update on 01/23/1992, 1 field added/edited/deleted.

Complete Update on 05/21/1990, 1 field added/edited/deleted.
Complete Update on 04/16/1990, 2 fields added/edited/deleted.
Complete Update on 01/11/1990, 2 fields added/edited/deleted.
Field update on 12/29/1989, 1 field added/edited/deleted.
Complete Update on 07/28/1989, 85 fields added/edited/deleted.
Field Update on 05/05/1989, 1 field added/edited/deleted.
Complete Update on 08/15/1988, 102 fields added/edited/deleted.
Complete Update on 03/31/1986

METHYL ETHYL KETONE

CASRN: 78-93-3

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Evidence for Carcinogenicity
Human Toxicity Excerpts
Skin, Eye and Respiratory Irritations
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☐ Probable Routes of Human Exposure
☐ Body Burden
☐ Average Daily Intake
☐ Minimum Fatal Dose Level
☐ Emergency Medical Treatment
☐ Emergency Medical Treatment
☐ Antidote and Emergency Treatment
☐ Animal Toxicity Studies
☐ Evidence for Carcinogenicity
☐ Non-Human Toxicity Excerpts
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TOLUENE

CASRN: 108-88-3

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TOLUEN (CZECH)
PEER REVIEWED

Synonyms :

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PEER REVIEWED

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- Ecotoxicity Values
- TSCA Test Submissions
- Metabolism/Pharmacokinetics
- Metabolism/Metabolites
- Absorption, Distribution & Excretion
- Biological Half-Life
- Mechanism of Action
- Interactions
- Pharmacology
- Interactions
- Minimum Fatal Dose Level
- Environmental Fate & Exposure
- Environmental Fate/Exposure Summary
- Probable Routes of Human Exposure
- Body Burden
- Average Daily Intake
- Natural Pollution Sources
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- Environmental Fate
- Environmental Biodegradation
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- Environmental Bioconcentration
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- [ ] Environmental Standards & Regulations
- [ ] FIFRA Requirements
- [ ] TSCA Requirements
- [ ] CERCLA Reportable Quantities
- [ ] RCRA Requirements
- [ ] Atmospheric Standards
- [ ] Clean Water Act Requirements
- [ ] Federal Drinking Water Standards
- [ ] Federal Drinking Water Guidelines
- [ ] State Drinking Water Standards
- [ ] State Drinking Water Guidelines
- [ ] FDA Requirements
- [ ] Allowable Tolerances
- [ ] Chemical/Physical Properties
- [ ] Molecular Formula
- [ ] Molecular Weight
- [ ] Color/Form
- [ ] Odor
- [ ] Boiling Point
- [ ] Melting Point
- [ ] Corrosivity

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- ☐ Density/Specific Gravity
- ☐ Heat of Combustion
- ☐ Heat of Vaporization
- ☐ Octanol/Water Partition Coefficient
- ☐ Solubilities
- ☐ Spectral Properties
- ☐ Surface Tension
- ☐ Vapor Density
- ☐ Vapor Pressure
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☐ Chemical Safety & Handling

- ☐ DOT Emergency Guidelines
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- ☐ Skin, Eye and Respiratory Irritations
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- ☐ NFPA Hazard Classification
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- ☐ Flash Point
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- ☐ Firefighting Hazards
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- ☐ Hazardous Reactivities & Incompatibilities
- ☐ Hazardous Decomposition
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- Preventive Measures
- Shipment Methods and Regulations
- Storage Conditions
- Cleanup Methods
- Disposal Methods
- Occupational Exposure Standards
- OSHA Standards
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- NIOSH Recommendations
- Immediately Dangerous to Life or Health
- Other Occupational Permissible Levels
- Manufacturing/Use Information
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- U. S. Production
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- Analytic Laboratory Methods
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- Special References

- [ ] Special Reports
- [ ] Synonyms and Identifiers
- [ ] Synonyms
- [ ] Formulations/Preparations
- [ ] Shipping Name/ Number DOT/UN/NA/IMO
- [ ] Standard Transportation Number
- [ ] EPA Hazardous Waste Number
- [ ] RTECS Number
- [ ] Administrative Information
- [ ] Hazardous Substances Databank Number
- [ ] Last Revision Date
- [ ] Last Review Date
- [ ] Update History
- [ ] Record Length

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2 Non-Human Toxicity Excerpts
3 Human Toxicity Excerpts
4 Non-Human Toxicity Excerpts
5 Metabolism/Metabolites
6 Mechanism of Action
7 Non-Human Toxicity Excerpts
8 Mechanism of Action
9 Human Toxicity Excerpts
10 Human Toxicity Excerpts
11 Human Toxicity Excerpts
12 Human Toxicity Excerpts
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TOLUENE DIISOCYANATE

CASRN: 26471-62-5

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Best Sections

Non-Human Toxicity Excerpts :

The effect of exposure to **toluene** diisocyanate vapor on pulmonary performance was studied in guinea pigs. Female English smooth haired guinea pigs were exposed to 1.4 ppm **toluene** diisocyanate vapor or air for 3 hours per day for 4 days, or to 0.02 ppm **toluene** diisocyanate for 6 hours per day for 70 days. Pulmonary performance was evaluated by the ventilatory response of the animals to 10% carbon dioxide. Serum antibodies to **toluene** diisocyanate were measured on days 22 and 50 and **toluene** diisocyanate pulmonary hypersensitivity was measured on days 37 and 38. Lung tissue histopathology was evaluated in all animals on day 50 following **toluene** diisocyanate exposure. Pulmonary response to 10% carbon dioxide diminished by 30 to 50% following **toluene** diisocyanate exposures at 1.4 ppm up to day 14. The ventilatory response showed recovery during the next 5 weeks. In contrast, animals exposed to 0.02 ppm **toluene** diisocyanate daily for 70 days showed no change in ventilatory response, nor did control animals that were not exposed to **toluene** diisocyanate. Antibodies were detected on day 22 and pulmonary hyprsensitivity to **toluene** diisocyanate was found in all animals exposed to 1.4 ppm **toluene** diisocyanate. No antibodies to **toluene** diisocyanate nor pulmonary hypersensitivity were detected in animals exposed to 0.02 ppm **toluene** diisocyanate or in control animals. Lung tissue on day 50 in the 1.4 ppm **toluene** diisocyanate exposed animals showed multifocal subchronic interstitial inflammation, localized pleural thickening, and peripheral lymphoid hyperplasia. No apparent abnormalities were observed in lung tissue of the 0.02 ppm exposed group. Exposure to 1.4 or 0.02 ppm **toluene** diisocyanate resulted in measurable and no apparent pulmonary toxicity in guinea pigs, respectively. The 10 percent carbon dioxide challenge provide several advantages for measuring pulmonary function.
[Wang KL et al; J Toxicol Environ Health 15 (1): 137-48 (1985)]**PEER REVIEWED**

Non-Human Toxicity Excerpts :

Exposing guinea pigs to **toluene** diisocyanate causes an acute increase in airway responsiveness to inhaled acetylcholine. The mechanism of this increase in airway responsiveness is unknown. Capsaicin-sensitive afferent nerves and the tachykinins they release upon activation are important in controlling bronchomotor tone in guinea pigs. To determine whether tachykinins are important in **toluene** diisocyanate induced airway hyperresponsiveness, the effects of tachykinin depletion were studied using capsaicin, and competitive tachykinin antagonism, using (D-Argl, D-Pro2, D-Trp7.9, Leull) substance P, on **toluene** diisocyanate induced airway hyperresponsiveness. In 9 of 9 untreated animals, **toluene** diisocyanate exposure caused a large and significant increase in airway responsiveness to acetylcholine. The mean concentration of acetylcholine required to decrease specific airway conductance by 50% below baseline (the PD50) was 1.51% before **toluene** diisocyanate exposure and 0.17% after **toluene** diisocyanate exposure ($p < 0.0005$). Capsaicin treatment had no effect on the PD50 but prevented the **toluene** diisocyanate induced increase in airway responsiveness in 10 of 12 animals. (The PD50 was 1.03% before **toluene** diisocyanate and 1.27% after **toluene** diisocyanate exposure.) Treatment with the tachykinin antagonist (D-Argl, D-Pro2, D-Trp7.9, Leull) substance P also abolished the **toluene** diisocyanate induced increase in airway responsiveness in all 5 animals treated. Although **toluene** diisocyanate exposure also caused airway edema, the effect of capsaicin treatment on **toluene** diisocyanate induced hyperresponsiveness did not result from prevention of airway edema. **Toluene** diisocyanate exposure caused a marked increase in tracheal extravasation of intravenously administered Evans blue dye that was not prevented by capsaicin

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treatment.
[Thompson JE et al; Am Rev Respir Dis 136 (1): 43-9 (1987)]**PEER REVIEWED**

Human Toxicity Excerpts :

The presence of different thresholds on bronchial reactivity to **toluene** diisocyanate was tested in 20 spray painters employed in the furniture industry and affected by TDI induced asthma. Bronchial provocation tests failed to demonstrate nonspecific hyperreactivity to methacholine. Exposure of the workers to **toluene** diisocyanate in concentrations ranging from 0.02 to 0.25 ppm demonstrated the occurrence of low, moderate and high thresholds of airways response to **toluene** diisocyanate in nine, seven and four patients, respectively. There was no association between the **toluene** diisocyanate response threshold and the positive response pattern to the lower range of **toluene** diisocyanate levels, but six of the nine patients with low threshold of response to **toluene** diisocyanate and six of the 11 patients with moderate or high thresholds had nonspecific bronchial hyperreactivity. The response to **toluene** diisocyanate also was not associated with the duration of the asthmatic condition, smoking, cessation of work or nonspecific response to methacholine. The pattern of response was not dose dependent in ten of 13 patients who had two positive bronchial provocation tests with different levels of **toluene** diisocyanate, although dual responses were recorded in three patients who had late reactions at low concentrations of **toluene** diisocyanate. The value of forced expiratory volume in one second, recorded during immediate reactions, showed a dose response relationship, in that it declined by 28.4% at lower **toluene** diisocyanate levels as compared to 38.3% following inhalation of higher doses of the compound; no such association was established for the late reaction to **toluene** diisocyanate. The results conclude that patients who are sensitive to **toluene** diisocyanate may have different thresholds of response to the agent.
[Paggiaro PL et al; Respiration 50 (3): 167-73 (1986)]**PEER REVIEWED**

Non-Human Toxicity Excerpts :

Groups of 50 F344/N rats of each sex and 50 B6C3F1 mice of each sex were gavaged with corn oil or a mixture of **toluene** diisocyanate in corn oil for 5 days per wk for 105 or 106 wk. Female rats and mice were given doses of 60 or 120 mg/kg body weight, while male rats received 30 or 60 mg/kg, and male mice received 120 or 240 mg/kg. The **toluene** diisocyanate reacted with the moisture in the corn oil vehicle resulting in doses that were 10% to 23% below the target dose concn. The chemical product used was commercial grade **toluene** diisocyanate, which was an 80%-20% mixture of the 2,4- and 2,6-isomers. Chemical disposition and metabolism studies were conducted with each of the radiolabelled **toluene** diisocyanate isomers in male rats. Absorption of both of the **toluene** diisocyanate isomers occurred, with the highest concn found in the stomach, cecum, large intestine, and bladder. Excretion occurred via the feces and urine. The major metabolic products from the metabolism of 2,4-**toluene** diisocyanate were shown to be identical with those from the metabolism of the carcinogen, 2,4-diaminotoluene, whereas the metabolism of the 2,6-**toluene** diisocyanate isomer yielded one major product, identified as 2,6-bis(acetylamino)**toluene**. Greater than 10% depression in body weight gain occurred in all dosed groups of rats throughout most of the study. The major non-neoplastic lesions that were observed in both sexes of the **toluene** diisocyanate exposed rats were dose related incr in acute broncho-pneumonia, characterized as chemical pneumonitis, with incidences as high as 50%. In mice mean body weight gain was depressed in dosed male and in high dose females. The principle non-neoplastic lesion in mice that was attributed to chemical treatment was cytomegaly of the kidney tubular epithelium in males. Survival in all groups of dosed rats was significantly lower than in controls. A dose-dependent pattern of mortality did not commence until 70 wk of exposure, demonstrating that **toluene** diisocyanate elicited a cumulative toxic response. There was also significantly lower survival in high dose male, but not female mice, by comparison to controls. Despite the reduction of power and sensitivity in the rat studies caused by early mortality, statistically significant incr in tumor incidences were observed in many different target organs. **Toluene** diisocyanate was carcinogenic in F344/N rats, causing sc fibromas and fibrosarcomas in males and females, pancreatic acinar cell adenomas in males, and pancreatic islet cell adenomas, neoplastic nodules of the liver, and mammary gland tumors in females.
[Dieter MP et al; Toxicol Ind Health 6 (6): 599-621

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(1990)]**PEER REVIEWED**

Metabolism/Metabolites :

It has been previously shown that tachykinin depletion or antagonism prevented the increase in airway responsiveness to inhaled acetylcholine caused by exposure to **toluene** diisocyanate in awake guinea pigs. To insure that the effects of tachykinins were not limited to the extrathoracic airways and were not dependent on effects of **toluene** diisocyanate on baseline airway caliber, airway responsiveness to acetylcholine inhaled through tracheostomy in anesthetized and ventilated guinea pigs that were exposed to **toluene** diisocyanate or air after treatment with the tachykinin antagonist spantide, the tachykinin metabolism inhibitor phosphoramidon, or the vehicles for each drug were determined. When these drugs were administered before and during **toluene** diisocyanate exposure, spantide significantly inhibited the **toluene** diisocyanate induced increase in acetylcholine responsiveness and phosphoramidon significantly potentiated this effect, whereas neither drug altered acetylcholine responsiveness in air exposed animals. To determine whether tachykinins were exerting their effect primarily during **toluene** diisocyanate exposure or during the subsequent acetylcholine challenge, the effect of each drug on acetylcholine responsiveness was also examined when the drugs were given after **toluene** diisocyanate exposure. At that time, spantide did not inhibit **toluene** diisocyanate induced acetylcholine hyperresponsiveness and phosphoramidon did not potentiate it. Neither drug nor **toluene** diisocyanate increased pulmonary resistance measured through a tracheostomy in these anesthetized and ventilated animals. These results suggest that the **toluene** diisocyanate induced increase in acetylcholine responsiveness is mediated by release of tachykinins into the intrathoracic airways during exposure to **toluene** diisocyanate.
[Sheppard D, Scypinski L; Am Rev Respir Dis 138 (3): 547-51 (1988)]**PEER REVIEWED**

Mechanism of Action :

The effects of **toluene** diisocyanate on T-cell subpopulations and circulating lymphocytes in ten persons (five males)): 19 to 50 yr old, with **toluene** diisocyanate induced occupational asthma were examined. Five subjects revealed early and late asthmatic reactions to **toluene** diisocyanate (dual responders) and five revealed late asthmatic reactions (late responders). Subjects underwent inhalation challenge with 0.005 to 0.015 ppm **toluene** diisocyanate or filtered air for 10 to 30 min on two occasions. One second forced expiratory volumes were measured before and at periodic intervals between 30 min and 24 hr after challenge. Venous blood samples were drawn 30 min and 8, 24, 48, and 72 hr after **toluene** diisocyanate. Total and differential leukocyte counts and T-cell subpopulations were determined. The five dual responders demonstrated forced expiratory volume in 1 sec decreased indicative of early and late asthmatic reactions and the five late responders demonstrated forced expiratory volume in 1 second decr indicative of a late asthmatic reaction. **Toluene** diisocyanate challenge did not affect the number of circulating erythrocytes and leukocytes. The percentage of eosinophils was significantly increased 24 hr after challenge and sustained for up to 48 hr. The percentages of neutrophils, lymphocytes, and monocytes were not altered by **toluene** diisocyanate. Among the T-lymphocyte subpopulation, the proportion of CD8(+) lymphocytes was significantly increased 8 hr after **toluene** diisocyanate challenge. The increase was more pronounced in the lat responders. An additional increase in CD8(+) lymphocytes occurred 48 hr post exposure in seven subjects but was unrelated to responder type. The number of CD4(+) cells did not change. This resulted in a decrease in the CD4(+)/CD8(+) ratio 8 and 48 hr after **toluene** diisocyanate challenge. It was concluded that **toluene** diisocyanate induced late asthmatic reactions are associated with an increase in the number of suppressor/cytotoxic lymphocytes and eosinophils in peripheral blood.
[Finotto S et al; Br J Ind Med 48 (2):116-21 (1991)]**PEER REVIEWED**

Non-Human Toxicity Excerpts :

Toluene diisocyanate is a causative agent in occupational asthma. Through an oral catheter **toluene** diisocyanate, 0.03 ul, dissolved in 0.02 ml olive oil, was superfused on the tracheobronchial mucosa of anaesthetized guinea pigs. **Toluene** diisocyanate induced plasma exudation into both airway tissue and lumen (peak effect: 5 hr; duration approximately 17 hr). Light microscopy examinations demonstrated that the epithelium was not disrupted by this

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process (and that microvessels are abundant just beneath the epithelium). At days 6 and 21 after exposure to **toluene** diisocyanate PAS-positive cells were increased, but no other histological alterations were found. Also, the occurrence of peptide containing nerve fibres was not altered by **toluene** diisocyanate. After **toluene** diisocyanate exposure the airway smooth muscle tone was elevated as examined in vitro at base-line and at conc response to carbachol. The largest incr in tone were recorded 21 days after exposure to **toluene** diisocyanate. The abnormally large tone was not associated with an increased thickness of the smooth muscle layer nor was it associated with reduced effects of either beta 2-agonist (terbutaline) or xanthine (theophylline) relaxants. It is concluded that **toluene** diisocyanate induced plasma exudation into guinea pig airways for 17 hr without disrupting the epithelial lining and without causing major changes in the airway peptidergic innervation. Both the airway tone, and the number of mucous cells, are increased for at least 3 wk after exposure to **toluene** diisocyanate.
[Persson CG et al; Clin Exp Allergy 21 (6): 715-24 (1991)]**PEER REVIEWED**

Mechanism of Action :

Serum neutrophil chemotactic activity, which is associated with mast cell or basophil activation, was quantitated to determine if mast cell or basophil mediators are released during bronchoprovocation-inhalation challenge with subirritant levels of **toluene** diisocyanate. Four subjects with suspected **toluene** diisocyanate induced asthma and four mite-sensitive subjects with asthma who served as a comparison group were studied. neutrophil chemotactic activity was measured in a multiwell, microchemotaxis chamber. Blood samples were collected, and forced expiratory volume in 1 second measurements were performed before challenge and at regular intervals during the subsequent 24 hr. Three of four workers clinically sensitive to **toluene** diisocyanate reacted to a subirritant **toluene** diisocyanate exposure. There was no increase in neutrophil chemotactic activity during placebo challenges. neutrophil chemotactic activity increased in the three **toluene** diisocyanate sensitive workers during early and late asthmatic reactions in quantities proportional to the forced expiratory volume in 1 second decline. No increase in neutrophil chemotactic activity was found during **toluene** diisocyanate exposures in the **toluene** diisocyanate negative worker. Gel filtration analysis demonstrated the main neutrophil chemotactic activity fraction eluted with macromolecules of an estimated molecular weight greater than 440,000 daltons. This characteristic is compatible with neutrophil chemotactic factor of basophil or mast cell origin. The kinetics of neutrophil chemotactic activity release were similar in mite- and **toluene** diisocyanate induced asthmatic reactions. A high correlation (r = 0.97; p = 0.0006) was obtained between the percent decrease in forced expiratory volume in 1 second during early asthmatic reactions and percent increase in neutrophil chemotactic activity. These observations support the hypothesis that activation of mast cells or basophils is associated with **toluene** diisocyanate induced early and late asthmatic reaction.
[Sastre J et al; J Allergy Clin Immunol 85 (3): 567-72 (1990)]**PEER REVIEWED**

Human Toxicity Excerpts :

Two men were exposed to **toluene** diisocyanate atmospheres at three different air concn (ca 25, 50 and 70 ug/cu m). The **toluene** diisocyanate atmospheres were generated by a gas-phase permeation method, and the exposures were performed in an 8-cu m stainless-steel test chamber. The effective exposure period was 4 hr. The isomeric composition of the air in the test chamber was 30% 2,4-**toluene** diisocyanate and 70% 2,6-**toluene** diisocyanate. The concn of **toluene** diisocyanate in air of the test chamber was determined by an HPLC method using the 9-(N-methyl-amino-methyl)-anthracene reagent and by a continuous-monitoring filter-tape instrument. Following the hydrolysis of plasma and urine, the related amines, 2,4-toluenediamine and 2,6-toluenediamine, were determined as pentafluoropropionic anhydride derivatives by capillary gas chromatography using selected ion monitoring in the electron impact mode. In plasma, 2,4- and 2,6-toluenediamine showed a rapid-phase elimination half-time of ca 2-5 hr, and that for the slow phase was greater than 6 days. A connection was observed between concn of 2,4- and 2,6-**toluene** diisocyanate in air and the levels of 2,4- and 2,6-toluenediamine in plasma. The cumulated amount of 2,4-toluenediamine excreted in the urine over 24 hr was ca 15%-19% of the estimated inhaled dose of 2,4-**toluene** diisocyanate, and that of 2,6-toluenediamine was ca 17%-23% of the inhaled dose of 2,6-**toluene**

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diisocyanate. A connection was found between the cumulated (24 hr) urinary excretion of 2,4- and 2,6-toluenediamine and the air concn of 2,4- and 2,6-**toluene** diisocyanate in the test chamber.
[Brorson T et al; Int Arch Occup Environ Health 63 (4): 253-9 (1991)]**PEER REVIEWED**

Human Toxicity Excerpts :

The mechanism by which late asthmatic reactions are induced by **toluene** diisocyanate, a low molecular weight chemical that causes occupational asthma in exposed subjects, is unknown. An investigation was conducted to determine whether early and late asthmatic reactions induced by **toluene** diisocyanate are associated with changes in airway responsiveness to methacholine and airway inflammation as determined by bronchoalveolar lavage. Forced expiratory volume in 1 second was measured before and at regular intervals after exposure to **toluene** diisocyanate and dose-response curves to methacholine and bronchoalveolar lavage at 8 hr after **toluene** diisocyanate /were performed/ in a group of 6 subjects with late asthmatic reactions and in 6 subjects with only early asthmatic reactions. The same procedure was followed 2 hr after **toluene** diisocyanate in a group of 6 subjects with previously documented late asthmatic reactions and in a group of 6 subjects without any previously documented asthmatic reaction after **toluene** diisocyanate. In subjects with late asthmatic reactions, neutrophils were increased at both 2 hr and 8 hr and eosinophils and airway responsiveness were increased only at 8 hr. By contrast, neutrophils, eosinophils and airway responsiveness were not increased at 8 hr after **toluene** diisocyanate in subjectswith an early asthmatic reaction or at 2 hr after **toluene** diisocyanate in normal control subjects. These results suggest that late asthmatic reactions to **toluene** diisocyanate, and the associated increase in airway responsiveness may be caused by airway inflammation.
[Fabbri LM et al; Am Rev Respir Dis 136 (1): 36-42 (1987)]**PEER REVIEWED**

Human Toxicity Excerpts :

Six workers with occupational asthma due to **toluene** diisocyanate were studied. For each worker a detailed clinical and occupational history was taken, and lung function measurement and skin intradermal tests for common allergens were carried out. Methacholine inhalation challenge was performed before **toluene** diisocyanate inhalation, and 8 hr after **toluene** diisocyanate inhalation. Methacholine challenge was within normal limits when performed before **toluene** diisocyanate inhalation, but went into the asthmatic range after **toluene** diisocyanate inhalation. These cases provid evidence that asthma can be induced by **toluene** diisocyanate in the absence of airway hyperresponsiveness. They further demonstrate that an isolated negative methacholine inhalation test cannot be used to exclude sensitization to **toluene** diisocyanate. Screening and follow-up studies on workers exposed on **toluene** diisocyanate require serial measurements of airway responsiveness and of variable air-flow obstruction.
[Mapp CE et al; Eur J Respir Dis 68 (2): 89-95 (1986)]**PEER REVIEWED**

Human Toxicity Excerpts :

Forty-three workers exposed to low levels of **toluene** diisocyanate during the process of producing polyurethane forms were examined immunologically for immunoglobulin-G, A, M, and E and serum enzyme activities such as serum angiotensin converting enzyme, serum lysozyme and glycylproline dipeptidyl aminopeptidase. Air concn of **toluene** diisocyanate was annually measured in various places of work during the past five years from 1979 to 1983. The results obtained in the present study were as follows. The air concn of **toluene** diisocyanate at all places of work was below the permissible concn level of 0.02 ppm throughout the study period. Subjective symptoms and abnormal findings on chest X-ray considered directly related to **toluene** diisocyanate exposure were no observed. No remarkable abnormal findings in blood cell counts and in serum biochemical studies could be seen in any of the workers. The serum immunoglobulin-G levels in workers directly exposed to **toluene** diisocyanate were significantly higher ($p < 0.05$) than those in workers indirectly exposed to **toluene** diisocyanate and in non-exposed workers. In the study of serum enzymatic activity, serum lysozyme activity in workers exposed directly to **toluene** diisocyanate was significantly higher ($p < 0.01$) than those in workers indirectly exposed to **toluene** diisocyanate and in non-exposed workers.

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[Taniwaki H et al; Sangyo Igaku 29 (2): 130-5 (1987)]**PEER REVIEWED**

Metabolism/Metabolites :

Five men were exposed to **toluene** diisocyanate atmospheres for 7.5 hr. The **toluene** diisocyanate atmospheres were generated by a gas-phase permeation method, and the exposures were performed in an 8 cu m stainless steel test chamber. The mean air concn of **toluene** diisocyanate was ca 40 ug/cu m, which corresponds to the TLV of Sweden. The inhaled doses of 2,4- and 2,6-**toluene** diisocyanate were ca 120 ug. **Toluene** diisocyanate in the test chamber air was determined by an HPLC method using the 9-(N-methylaminomethyl)-anthracene reagent and by a continuous monitoring filter-tape instrument. After hydrolysis of plasma and urine, the related amines, 2,4- and 2,6-toluenediamine 2,4-, and 2,6-TDA), were determined as pentafluoropropionic anhydride derivatives by capillary gas-chromatography using selected ion monitoring in the electron-impact mode. The urinary elimination of the toluenediamines showed a possible biphasic pattern, with rapid first phases for 2,4-toluenediamine (mean half-life for the concn in urine, 1.9 hr) and for 2,6-toluenediamine (mean half-life for the concn in urine, 1.6 hr). The cumulative amount of 2,4-toluenediamine excreted in urine within 28 hr ranged from 8% to 14% of the estimated dose of 2,4-**toluene** diisocyanate, and the cumulative amount of 2,6-toluenediamine in urine ranged from 14% to 18% of the 2,6-**toluene** diisocyanate dose. The average urinary level of 2,4-toluenediamine was 5 ug/l in the 6 to 8 hr sample (range 2.8-9.6 ug/l), and the corresponding value fo 2,6-toluenediamine was 8.6 ug/l (range, 5.6-16.6 ug/l). Biological monitoring of exposure to 2,4- and 2,6-**toluene** diisocyanate by analysis of 2,4- and 2,6-toluenediamine in urine is feasible.
[Skarping G et al; Int Arch Occup Environ Health 63 (2): 83-8 (1991)]**PEER REVIEWED**

Human Toxicity Excerpts :

To determine whether late asthmatic reactions and the associated increase in airway induced by **toluene** diisocyanate are linked to airway inflammation, inhibition by prednisone was investigated. Ten "sensitized" subjects were studied in 2 sets of experiments. In the first set, each subject was given no treatment and was studied before and for 8 hr after exposure to **toluene** diisocyanate. In the second set, 2 to 4 wk later, each subject was studied before treatment and then during treatment with prednisone (50 mg once a day for 3 days, orally), both before and after exposure to **toluene** diisocyanate. To assess late asthmatic reactions to **toluene** diisocyanate FEV1 /was measured/ immediately before and after exposure, then hourly for 8 hr. To assess changes in airway responsiveness, a /measurement was made of/ the provocation dose (mg) of methacholine causing a 20% decrease in FEV1 (PD20FEV1) before and 8 hr after exposure to **toluene** diisocyanate. When the subjects received no prednisione treatment, **toluene** diisocyanate caused late asthmatic reactions and increased airway responsiveness. By contrast, when the subjects received prednisone, **toluene** diisocyanate caused no late asthmatic reaction or increased airway responsiveness. Prednisone did not change baseline airway caliber or airway responsiveness. These results suggest that late asthmatic reactions and the associated increase in airway responsiveness induced by **toluene** diisocyanate in "sensitized" subjects may depend on the development of a steroid-responsive acute inflammatory reaction within the airways.
[Fabbri LM; Am Rev Respir Dis 132 (5): 1010-4 (1985)]**PEER REVIEWED**

Human Toxicity Excerpts :

A worker developed **toluene** diisocyanate induced asthma in 1974. On reassessment, 11 yr after leaving the chemical plant where **toluene** diisocyanate was produced, he had no respiratory symptoms and normal bronchial reactivity in response to methacholine, and showed no reaction when challenged with a subirritant concn of **toluene** diisocyanate. He developed asthma within five months of returning to the workplace. Repeat challenge testing showed bronchial hyperreactivity to methacholine and to the specific sensitising agent, **toluene** diisocyanate. This clinical pattern could be due to underlying **toluene** diisocyanate sensitivity with resolution and reappearance of hyperresponsiveness to methacholine and **toluene** diisocyanate reactivity associated with workplace **toluene** diisocyanate exposure. Alternatively, this worker may have developed sensitisation to **toluene** diisocyanate anew.
[Banks DE, Rando RJ; Thorax 43 (8): 1988 660-2]**PEER REVIEWED**

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Mechanism of Action :

Leukotriene B4 release from the lungs of sensitized subjects during asthmatic reactions induced by **toluene** diisocyanate was investigated. Three groups of **toluene** diisocyanate sensitized subjects were examined, one after no exposure to **toluene** diisocyanate, the second 8 hr after an exposure to **toluene** diisocyanate that caused an early asthmatic reaction, and the third 8 hr after an exposure to **toluene** diisocyanate that caused a late asthmatic reaction. Bronchoalveolar lavage fluid was analysed by reverse-phase HPLC and by specific radioimmunoassay. The mean concn of leukotriene B4 was higher (0.31 + or - 0.09 (standard error) ng/ml, range 0.15-0.51) in bronchoalveolar lavage fluid of sensitized subjects who developed a late asthmatic reaction than in bronchoalveolar lavage fluid of subjects who developed an early asthmatic reaction (0.05 + or - 0.04 ng/ml, range 0-0.224), and no leukotriene B4 was detectable in the control subjects. Bronchoalveolar lavage was also performed 8 hr after **toluene** diisocyanate exposure on four **toluene** diisocyanate sensitized late-dual reactors who were on steroid treatment. In this group of subjects no leukotriene B4 was detectable. These results suggest that leukotriene B4 may be involved in late asthmatic reactions induced by **toluene** diisocyanate.
[Zocca E et al; J Appl Physiol 68 (4): 576-80 (1990)]**PEER REVIEWED**

Interactions :

The effects of methacholine inhalation on airway responsiveness in **toluene** diisocyanate induced asthma were studied in six workers with a history of sensitivity to **toluene** diisocyanate. Symptoms among subjects included shortness of breath, wheezing, cough, and chest tightness at work, during the evening, or at night. A detailed cllnical and occupational history was taken for each subject, and lung function measurement and skin intradermal tests for common allergens were conducted. Airway responsiveness to methacholine was assessed before subjects were exposed for 30 minutes to 0.02 part per million **toluene** diisocyanate in an exposure chamber. Eight hours after **toluene** diisocyanate inhalation, airway responsiveness to methacholine was again determined. Forced expiratory volume was the measure of airway responsiveness. Although methacholine challenge was within normal limits when performed before **toluene** diisocyanate inhalation, the challenge went into the asthmatic range after **toluene** diisocyanate inhalation. Airway responsiveness increased significantly 8 hours after **toluene** diisocyanate challenge in the subjects and was accompanied by a decrease in forced expiratory volume. The late asthmatic reaction began between 3 and 5 hours asthma can be induced by **toluene** diisocyanate in the absence of airway responsiveness.
[Mapp CE et al; Eur J Respir Dis 68: 89-95 (1986)]**PEER REVIEWED**

Protective Equipment & Clothing :

Three commercial air-purifying respirators for protection against **toluene** diisocyanate vapors were evaluated. The Willson R-21 and Survivair, organic vapor cartridges, and the disposable, valveless 3M-8711 were the three respirators evaluated. Each respirator/cartridge was tested three times at 0.2 ppm **toluene** diisocyanate concn for 40 hr and once for 20 hr or more at concn greater than 1.5 ppm **toluene** diisocyanate. All cartridges/respirators had the capacity to provide the required protection against **toluene** diisocyanate vapors. Additional considerations in the respirator selection process included the training and experience of the respirator user, the enforcement of the respirator program, fit of the respirator, knowledge of **toluene** diisocyanate concn onsite, presence of other solvents or chemicals in the air which may adversely affect the capacity of the respirato for **toluene** diisocyanate, and the high odor threshold of **toluene** diisocyanate that makes it impossible for the user to receive advance warning of a leak.
[Dharmarajan V et al; Am Ind Hyg Assoc 47 (7): 393-8 (1986)]**PEER REVIEWED**

Analytic Laboratory Methods :

A solvent free sampling method for airborne **toluene** diisocyanate was described. Air samples were collected on quartz fiber filters impregnated with 1-(2-methoxyphenyl)piperazine. **Toluene** diisocyanate in the samples reacted with 1-(2-methoxyphenyl)piperazine to form urea derivatives which after dissolution in methanol were analyzed by reversed or normal phase HPLC. When reversed phase HPLC was used, a C18 bonded phase column was utilized. A

- Hazardous Substances Databank Number
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- Update History
- Record Length

cyano amino bonded phase column was used with normal phase HPLC. An ultraviolet detector set at a wavelength 250 nanometers was also used. Detection limits for a 15 liter air sample based on a 5 mm peak height were 0.02 to 0.04 mg/cu m, corresponding to 0.5 to 1 nanograms of **toluene** diisocyanate injected. The method was used to sample laboratory generated **toluene** diisocyanate containing atmospheres over the relative humidity range 11 to 75% and temperature range 20 to 50 deg C. In the study of the effects of humidity, samples were also collected with gas bubblers and silica gel tubes for comparison purposes. **toluene** diisocyanate concn in the collected samples increased linearly with incr temperature. When the samples were collected on the 1-(2-methoxyphenyl)piperazine coated fibers the collected **toluene** diisocyanate concn were not affected by changes in relative humidity. Collection efficiency of the bubblers and silica gel tubes decr for humidities in excess of 45%. It was concluded that the 1-(2-methoxyphenyl)piperazine impregnated quartz fiber filter method for **toluene** diisocyanate sampling is convenient and efficient, and that collection efficiency does not appear to be affected by humidity.
[Robert A, Simon P; Chromatographia 23 (7):507-11 (1987)]**PEER REVIEWED**

Human Toxicity Excerpts :

An outbreak of occupational asthma due to **toluene** diisocyanate among industrial workers was described. Four employees at a velcro/like tape manufacturing factory in Taipei, Taiwan were seen in an outpatient clinic complaining of cough, shortness of breath, and wheezing. The symptoms became worse at night and improved after long holidays. The patients' job involved applying an adhesive to the tape. Thirty eight of 45 employees were interviewed by questionnaire and given pulmonary function tests. The pulmonary function tests were given during a workday, after a 10 day holiday, and 5 mo after control measures such as process isolation, improved ventilation, and substitution for **toluene** diisocyanate were instituted. Industrial hygiene sampling for **toluene** diisocyanate was conducted. Fourteen workers had symptoms of asthma or asthmatic bronchitis. The highest attack rate occurred in workers employed in the tape processing area where the adhesive was applied. Workers in the tape processing area also showed the greatest decr in 1 second forced expiratory volume and forced vital capacity over the workday. Mean **toluene** diisocyanate concn ranged from 0.012 to 0.047 ppm, the highest occurring in the tape processing area and the lowest in the weaving area. The prevalence of asthmatic symptoms was significantly correlated with **toluene** diisocyanate concn. The forced expiratory volume in 1 second and forced vital capacity values were significantly improved after the 10 day holiday and 5 mo after the control methods were instituted. No asthmatic symptoms were reported after 5 mo. It was concluded that **toluene** diisocyanate was responsible for the outbreak and improving the work environment was effective in reducing exposure to **toluene** diisocyanate.
[Wang JD et al; Am J Ind Med 14 (1): 73-8 (1988)]**PEER REVIEWED**

Human Toxicity Excerpts :

The effect of cessation of exposure to **toluene** diisocyanate was studied in six patients with **toluene** diisocyanate induced asthma, proved by a positive inhalation challenge with **toluene** diisocyanate. Bronchial challenges with **toluene** diisocyanate and methacholine were performed, and lobar bronchial biopsies were taken at diagnosis and 6 mo later, after cessation of exposure. Biopsies from four nonasthmatic control subjects were also examined. At diagnosis, asthmatic subjects had thickened reticular basement membrane ($p < 0.05$) and increased numbers of mononuclear cells ($p < 0.05$) and eosinophils ($p < 0.05$) in the lamina propria when compared with control subjects. Electron microscopy showed degranulation of eosinophils and mast cells in asthmatics. Six months after cessation of exposure, the thickness of reticular basement membrane was significantly reduced compared with that at diagnosis ($p < 0.05$), and it decr to values similar to those of control biopsies. Inflammatory cell numbers in bronchial mucosa of asthmatic subjects did not change significantly 6 mo after removal from exposure, and degranulation of eosinophils and mast cells was still present. At the end of the study, airwa hyperresponsiveness to methacholine and/or sensitivity to **toluene** diisocyanate persisted in most of the asthmatic patients despite the cessation of exposure and the disappearance of asthmatic symptoms. In conclusion, in patients with occupational asthma induced by **toluene** diisocyanate, the avoidance of exposure to the sensitizing agent for 6 mo is

able to reverse the reticular basement membrane thickening in the bronchial mucosa, but th inflammatory cell infiltrate, the specific sensitivity to **toluene** diisocyanate, and the nonspecific airway hyperreactivity may persist.
[Saetta M et al; Am Rev Respir Dis 145 (1): 169-74 (1992)]**PEER REVIEWED**

Human Toxicity Excerpts :

Among the painters handling polyurethane varnish in two furniture manufacturing factories with high **toluene** diisocyanate exposure (0.79 mg/cu m and 0.31 mg/cu m), 26.3% and 15% subjects, respectively displayed asthmatic symptoms, lung function loss, and an increment in mast cell degranulation percentage specific to **toluene** diisocyanate. Some cases of **toluene** diisocyanate linked contact dermatitis were also found among them, being elucidated by positive patch testing to **toluene** diisocyanate. However, the previous abnormalities could not be verified among the painters from another factory with **toluene** diisocyanate concn below the TLV of it (0.11 mg/cu m). It was concluded that both pulmonary hypersensitivity and contact sensitization to **toluene** diisocyanate had occurred in some of the painters included in this study, and that the immunologic effects of **toluene** diisocyanate was concn dependent.
[Huang J et al; Arch Environ Contam Toxicol 21 (4): 607-11 (1991)]**PEER REVIEWED**

Human Toxicity Excerpts :

Pulmonary function tests were done and compared to current and past potential exposure levels of **toluene** diisocyanate for 57 **toluene** diisocyanate manufacturing workers and 89 workers not exposed to **toluene** diisocyanate or other known respiratory hazards. The average **toluene** diisocyanate plant experience was 4.1 yr (standard deviation = 2.8). Routine industrial hygiene measurements have shown **toluene** diisocyanate exposure below a time-weighted average of 0.005 ppm and a short-term exposure level of 0.02 ppm. A certified industrial hygienist ranked department and job classification by level of potential exposure to **toluene** diisocyanate (none, low, moderate, and high). A questionnaire was administered to determine the prevalence of respiratory symptoms and smoking habits. Using backward regression analysis, cumulative pack-years of cigarette smoking and prevalence of lower respiratory symptoms were statistically significant predictors of a standardized forced expiratory volume at 1 second; however, **toluene** diisocyanate exposure, whether classified as current, highest career level, cumulative, or cumulative highest-to-date, was not associated with a decline in forced expiratory volume.
[Olsen GW et al; J Occup Med 31 (8): 664-7 (1989)]**PEER REVIEWED**

Mechanism of Action :

Isocyanates are an important cause of occupational asthma. The mechanism of isocyanate induced asthma is still unknown. To determine whether **toluene** diisocyanate stimulates the 'efferent' function of peripheral endings of capsaicin-sensitive sensory nerves, we investigated the effect of **toluene** diisocyanate in the rat isolated urinary bladder, a preparation in which the action of capsaicin has been well characterized. **Toluene** diisocyanate (0.03 mM) produced a concn dependent contraction of the bladder strips. It maximal effect was about 50 % of the response to capsaicin (1 uM). Previous exposure of the strips to capsaicin followed by washing out produced complete unresponsiveness, both to the first exposure to **toluene** diisocyanate and to a second exposure of capsaicin. Further, the response to both **toluene** diisocyanate and capsaicin was completely prevented by extrinsic bladder denervation, achieved by bilateral removal of pelvic ganglia (72 hr before). Repeated exposure of the rat bladder to **toluene** diisocyanate reduced the capsaicin-evoked release of calcitonin gene-related peptide like immunoreactivity (CGRP-LI), taken as biochemical marker of activation of these sensory nerves. These experiments provide the first evidence that **toluene** diisocyanate activates directly or indirectly the efferent function of capsaicin-sensitive primary sensory nerves.
[Mapp CE et al; Eur J Pharmacol 180 (1): 113-8 (1990)]**PEER REVIEWED**

Non-Human Toxicity Excerpts :

The **toluene** diisocyanate induced delayed type hypersensitivity reaction in the ear of male mice

was investigated and compared with the picryl chloride induced one. The results obtained were as follows: 1) When 1% **toluene** diisocyanate solution (20 ul/ear) as a challenging concentration was used for 7 week old ICR mice, distinct ear swelling was observed in every group sensitized with various concentrations (1-5%, 100 ul/animal) of **toluene** diisocyanate solution, and the swelling rate was the same or higher than that of picryl chloride induced delayed type hypersensitivity. 2) Five, 7 and 13 week old ICR mice showed a similar high response in TDI induced delayed type hypersensitivity, whereas the reactivity of 16 week old ICR mice was significantly lower than that of the above mentioned younger mice. 3) In both **toluene** diisocyanate and picryl chloride induced delayed type hypersensitivity reaction, ICR and BALB/c mice showed a similar high response, whereas the reactivity of ddY mice was significantly lower. The effects of dexamethasone and indomethacin were investigated with the **toluene** diisocyanate induced delayed type hypersensitivity model. The delayed type hypersensitivity reaction was suppressed significantly by both drugs, but the suppressive effects of dexamethasone were higher than that of indomethacin. All the above results indicate that the **toluene** diisocyanate induced delayed type hypersensitivity model in mice taking dye leakage as an index may be useful for evaluation of drugs for disorders derived from delayed type hypersensitivity reactions.
[Tominaga M et al; Jpn J Pharmacol 39 (2): 163-71 (1985)]**PEER REVIEWED**

Non-Human Toxicity Excerpts :

The changes in airway responsiveness to increasing doses of an acetylcholine aerosol in anesthetized and ventilated guinea pigs 2, 6, or 24 hr after exposure to air or 1 ppm **toluene** diisocyanate were examined. Pulmonary resistance after the animals inhaled a buffered saline aerosol was used as baseline and was similar for air and groups. The concentration of acetylcholine calculated to cause a 200% increase in pulmonary resistance was significantly lower for animals studied at 2 hr (0.68%) or at 6 hr (0.77%), but not at 24 hr (2.39%), after than for air animals (3.07%). The increase in airway responsiveness in the exposed animals was associated with histologic changes in the trachea and intrapulmonary airways. Exposure to 2 ppm caused a patchy loss of cilia, shedding of epithelial cells into the airway lumen, and an influx of inflammatory cells into the trachea and other airways. In the lamina propria of the trachea, the concentration of extravascular polymorphonuclear leukocytes was 13 to 26-fold greater in animals studied 2 or 6 hr after exposure to 2 ppm **toluene** diisocyanate or at 2 hr after 1 ppm **toluene** diisocyanate than in animals exposed to air. The concentration of polymorphonuclear leukocytes in the epithelium was significantly increased only in animals examined 2 hr after 2 ppm **toluene** diisocyanate. Exposure to **toluene** diisocyanate also caused an influx of eosinophils into the tracheal mucosa. This influx occurred later and was more persistent than the influx of polymorphonuclear leukocytes. These results indicate that a single exposure to **toluene** diisocyanate can cause an increase in airway responsiveness that is associated with epithelial injury and acute airwayinflammation.
[Gordon T et al; Am Rev Respir Dis 132 (5): 1106-12 (1985)]**PEER REVIEWED**

Human Toxicity Excerpts :

A study of individuals with occupational asthma induced by **toluene** diisocyanate was conducted. This was a followup of 35 patients, 25 males, with a history of isocyanate sensitization. They had 3 to 41 years' occupational exposure to isocyanate compounds. The subjects had been diagnosed with isocyanate asthma on the basis of their response to bronchial challenge with **toluene** diisocyanate. They were examined an average of 11 mo after diagnosis. They underwent bronchial challenge with **toluene** diisocyanate and methacholine. Forced expiratory volumes in 1 second were measured. Symptoms reported by the subjects were recorded. Twenty seven subjects were still asthmatic at followup as shown by a positive reaction to **toluene** diisocyanate challenge. They showed a deterioration in their forced expiratory volumes in 1 second and response to methacholine similar to that seen at diagnosis. Seventy seven percent of these subjects continued to have recurring attacks of dyspnea, wheezing, and cough which required medication. Twenty two of the asthma subjects had been removed from exposure. Subjects who recovered (did not react to **toluene** diisocyanate at the followup examination) showed an improvement in their forced expiratory volumes in 1 second and a reduced response to methacholine. At the time of diagnosis they tended to have an

immediate or dual asthmatic reaction and were younger than the other subjects. The asthmatic subjects had dual or late reactions at diagnosis. It was concluded that respiratory symptoms, isocyanate sensitization, and airway hyperresponsiveness may persist for some time after exposure to **toluene** diisocyanate has ended.
[Mapp CE et al; Am Rev Respir Dis 137 (6): 1326-9 (1988)]**PEER REVIEWED**

Metabolism/Metabolites :

A technique for detectingurinary amine metabolites in rats exposed to **toluene** diisocyanate was evaluated. Skin tissue of rats was exposed to 40% **toluene**-2,4-diisocyanate solution in di-n-butyl-ether liquid. Rats were exposed daily for 3 hr on 4 consecutive days. Urine was collected in metabolic cages for 18 hr after the last exposure. Chromatographic techniques were used for nitrogen selective detection of nonderivatized amines. An autolinear temperature programmer was employed to analyze derivatized amine. The identity of the amine was confirmed by gas chromatography/mass spectrometry. A linear correlation was found between **toluene**-2,4-diamine added to urine and peak height. Peak height and recovery from the non hydrolyzed and from the hydrolyzed urine was about 85 and 70%, respectively. No free **toluene**-2,4-diamine or free **toluene**-2,4-diisocyanate was detected in the urine of rats exposed to **toluene**-2,4-diamine in hydrolyzed urine was 1.5 micrograms per milliliter. Gas chromatography/mass spectrometry confirmed the identity of the amine. /This/ highly sensitive technique tested is easy to apply and is effective for trace assays of amines.
[Rosenberg C; J Chromatography 323 (2): 429-33 (1985)]**PEER REVIEWED**

Human Toxicity Excerpts :

Diisocyanate inhalation tests (maximal concn, 20 ppb; exposure time, 1-2 hr) were performed using **toluene** diisocyanate (TDI, n = 15) and diphenylmethane diisocyanate (MDI, n = 7) as well as methacholine challenges in 19 workers who had a clinical history of **toluene** diisocyanate/diphenylmethane diisocyanate induced asthma. Additionally volunteers were tested who had n previous contact with diisocyanates: 10 healthy individuals with a negative methacholine test and 14 patients with asthma and a positive methacholine test were exposed to **toluene** diisocyanate. In all, 1 of the normal volunteers and 3 of the patients with asthma unrelated to diisocyanates showed a positive airway reaction to **toluene** diisocyanate, and 13 of the 19 diisocyanate workers displayed a positive result in the **toluene** diisocyanate/diphenylmethane diisocyanate inhalation test; however, only 6 of these 13 individuals reacted to methacholine. Furthermore, 3 of the 6 patients with a negative **toluene** diisocyanate/diphenylmethane diisocyanate challenge test demonstrated a significant response to methacholine. It was concluded that bronchial hyperreactivity as evaluated by the methacholine challenge test is not closely related to isocyanate induced bronchoconstriction and, therefore, the metacholine challenge is only of limited diagnostic value in patients with suspected isocyanate induced asthma.
[Vogelmeier C et al; Int Arch Occup Environ Health 63 (1): 9-13 (1991)]**PEER REVIEWED**

Mechanism of Action :

To determine whether early and/or late asthmatic responses induced by **toluene** diisocyanate are caused by a reflex mechanism involving stimulation of muscarinic receptors, we studied the effect of the muscarinic antagonist atropine on early and late airway response induced by **toluene** diisocyanate. A preliminary study was conducted in asthmatics to assess whether the selected dose of atropine provided adequate muscarinic blockade. On different days we measured the provocation dose (in mg) of carbachol causing a 15% decrease in forced expiratory volume in 1 second (PD15FEV1) without and with atropine premedication (0.008 or 0.012 mg/kg sc atropine 30 or 90 min before carbachol challenge test). 0.008 to 0.012 mg/kg sc atropine increased the PD15FEV1 carbachol by 6 to 10 fold, inducing a consistent and prolonged decrease in nonspecific bronchial hyperresponsiveness to cholinergic agent. 10 Subjects with a history of sensitization to **toluene** diisocyanate were then examined in 2 sets of experiments. In the first set of experiments, the subjects were studied before and after exposure to **toluene** diisocyanate (0.04 ppm; 30 min) after no treatment. In the second set of experiments, carried out 1 to 2 wk later, the same procedure was repeated after treatment with atropine (0.008

to 0.012 mg/kg atropine sulfate administered sc 30 min before **toluene** diisocyanate challenge, and then at 90 min intervals after **toluene** diisocyanate exposure); all patients showed symptoms of atropine effect (dryness of mouth, cycloplegia, increased heart rate).
[Paggiaro P et al; Am Rev Respir Dis 136 (5): 1237-41 (1987)]**PEER REVIEWED**

Human Toxicity Excerpts :

An investigation of the persistence of isocyanate induced asthma in workers with negligible occupational exposure was carried out. Six asthmatic workers, proven to be **toluene** diisocyanate sensitive by inhalation challenge testing in a longitudinal study of respiratory health risks associated with polyurethane foam production, were examined. The subjects were followed for 5 yr during which they completed a respiratory symptom questionnaire annually. Pulmonary function and responsiveness to methacholine challenge were measured annually. **toluene** diisocyanate concn in their breathing zones were measured. After the original survey the six subjects were transferred to areas thought to have negligible **toluene** diisocyanate exposures. None of the subjects had respiratory or asthmatic complaints before they started work in polyurethane production. The respiratory symptoms of the subjects did not improve during the followup period. All six had bronchial hyperresponsiveness to methacholine that did not resolve over time. Three subjects demonstrated deficits in 1 second forced expiratory volume of greater than 15% on one of the testing days during the followup period. The need for less or additional asthma therapy of the subjects could not be predicted. The mean time weighted average **toluene** diisocyanate exposure experienced by the subjects was 0.64 ppb; less than 5% of the OSHA standard of 20 ppb. It was concluded that although the outcome of isocyanate induced asthma cannot be predicted, the asthmatic symptoms of these workers have persisted despite the negligible **toluene** diisocyanate exposures.
[Banks DE et al; Chest 97 (1): 121-5 (1990)]**PEER REVIEWED**

Non-Human Toxicity Excerpts :

THE POSSIBILITY OF DERMAL EXPOSURES TO **TOLUENE** DIISOCYANATE RESULTING IN PULMONARY SENSITIVITY WAS INVESTIGATED USING GUINEA PIGS AS AN ANIMAL MODEL. **TOLUENE** DIISOCYANATE (1-100% CONCN) WAS APPLIED TO DORSAL SITES ON GUINEA PIGS, WHERE SKIN SENSITIVITY TO TDI WAS APPARENT BY THE 7TH DAY. AFTER 14 DAYS, ANIMALS WERE ADDNL EVALUATED FOR TDI SENSITIVITY BY SEROLOGIC ANALYSIS & BRONCHIAL PROVOCATION CHALLENGE. ANTIBODIES TO **TOLUENE** DIISOCYANATE WERE DETECTED USING PASSIVE CUTANEOUS ANAPHYLAXIS, DOUBLE DIFFUSION IN GEL, & RADIOLABELED ANTIGEN BINDING ASSAYS. ANTIBODIES WERE SPECIFIC FOR **TOLUENE** DIISOCYANATE. THE DEVELOPMENT OF RESPIRATORY HYPERSENSITIVITY AS A RESULT OF DERMAL CONTACT WITH **TOLUENE** DIISOCYANATE EMPHASIZES THE IMPORTANCE OF CAREFUL WORKPLACE PRACTICES & SUGGESTS REEVALUATION OF THE ROLE OF INHALATION &/OR DERMAL CONTACT IN CAUSING PULMONARY SENSITIZATION OF WORKERS.
[KAROL MH ET AL; TOXICOL APPL PHARMACOL 58 (2): 221 (1981)]**PEER REVIEWED**

Mechanism of Action :

In order to determine whether treatment with ketotifen inhibits asthmatic reactions induced by **toluene** di-isocyanate, six sensitized subjects with previously demonstrated dual or late asthmatic reaction after inhalation challenge with **toluene** diisocyanate were studied. Ketotifen (1 mg bid, orally) or placebo was administered for 7 days to the examined subjects, according to a double-blind, cross-over, placebo controlled study design. When the subjects were treated with either ketotifen or placebo, forced expiratory volume in 1 second markedly decr after exposure to **toluene** diisocyanate. These results suggest that the anti-asthmatic agent ketotifen is not effective in **toluene** diisocyanate induced asthma and suggest that it should not be used in the prophylaxis of asthmatic reactions induced by **toluene** diisocyanate in sensitized subjects.
[Tossin L et al; Clin Exp Allergy 19 (2): 177-82 (1989)]**PEER REVIEWED**

Mechanism of Action :

To determine the importance of airway inflammation for the development of late asthmatic reactions, we examined sensitized subjects during late asthmatic reactions induced by exposure to **toluene** diisocyanate in the laboratory. Late asthmatic reactions are associated with a transient increase of bronchial responsiveness and, at the same time, with an increase of neutrophils followed by eosinophils, and of leukotriene B4 and albumin in bronchoalveolar lavage fluid. Late asthmatic reactions, increased bronchial responsiveness, and increase of neutrophils, eosinophils, leukotriene B4, and albumin concn in bronchoalveolar lavage induced by exposure to **toluene** diisocyanate are all prevented by pretreatment with prednisone but not with the nonsteroidal anti-inflammatory agent indomethacin. Aerosolized steroids (beclomethasone and dexamethasone isonicotinate) completely inhibit late asthmatic reactions induced by **toluene** diisocyanate, whereas theophylline has a partial, and verapamil, ketotifen, and cromolyn have no protective effect. These results suggest that late asthmatic reactions induced by **toluene** diisocyanate may be caused by airway inflammation, and that anti-inflammatory steroids should be recommended in the prophylaxis of **toluene** diisocyanate asthma.
[Fabbri LM et al; Am Rev Respir Dis 143 (3 Pt 2): 537-8 (1991)]**PEER REVIEWED**

Mechanism of Action :

The influence of cyclophosphamide induced granulocyte depletion on **toluene** diisocyanate related changes in airway reactivity and pathology was assessed in guinea pigs. Twelve cyclophosphamide-treated and 12 control animals comprising each group were studied physiologically before and 2 hr after a single 10 min exposure to 3 ppm of **toluene** diisocyanate. Reactivity was determined in intact unanesthetized animals by measuring specific airway conductance before and during intravenous acetylcholine infusion. After testing, tracheal tissue for light microscopic examination was obtained from three hyperreactive guinea pigs in each exposed group and compared with tissue from treated and control animals (n = 3 each) that had not been **toluene** diisocyanate exposed. Cyclophosphamide treatment caused substantial decr in both circulating and airway granulocyte counts. However, the incidence and degree of bronchial hyperreactivity that occurred 2 hr post-**toluene** diisocyanate was similar in the untreated and treated groups. Results indicate that **toluene** diisocyanate induced bronchial hyperreactivity 1) occurs shortly after a brief high concn exposure and 2) appears independent of circulating or airway granulocyte counts.
[Cibulas W Jr et al; J Appl Physiol 64 (5): 1773-8 (1988)]**PEER REVIEWED**

Mechanism of Action :

A study of the occurrence of serum immunoglobulin-E and immunoglobulin-G antibodies in workers with isocyanate induced asthma was conducted. The study group consisted of 62 workers (58 males) being evaluated for occupational asthma. Thirty nine had been exposed to hexamethylene diisocyanate, 17 to diphenylmethane diisocyanate, and six to **toluene** diisocyanate. The subjects completed a respiratory and occupational questionnaire. Spirometric tests were administered. Skin prick tests were performed with 15 common inhalant allergens and **toluene** diisocyanate, hexamethylene diisocyanate, and diphenylmethane diisocyanate human serum albumin conjugates. Blood samples were collected and assayed for specific serum immunoglobulin-G and immunoglobulin-E antibodies to hexamethylene diisocyanate, diphenylmethan diisocyanate, and **toluene** diisocyanate. Specific inhalation challenges were conducted with hexamethylene diisocyanate, diphenylmethane diisocyanate, and **toluene** diisocyanate. Specific inhalation challenge with **toluene** diisocyanate, hexamethylene diisocyanate, or diphenylmethane diisocyanate induced significant bronchoconstriction in half of the subjects, late reactions being the most common. Twenty subjects had significantly elevated immunoglobulin-G concn and nine had significantly elevated immunoglobulin-G plus immunoglobulin-E concn. Six of 12 subjects with elevated immunoglobulin-E and immunoglobulin-G antibodies had positive skin prick tests for hexamethylene diisocyanate and one was sensitized to diphenylmethane diisocyanate. It was concluded that an association between isocyanate specific antibodies and the results of specific inhalation challenge tests has been established. This suggests that isocyanate induced asthma may involve an immunological mechanism.
[Cartier A et al; J Allergy Clin Immunol 84 (4 Part 1): 507-14

(1989)]**PEER REVIEWED**

Mechanism of Action :

To investigate the role of pharmacological mechanisms in **toluene** diisocyanate induced occupational asthma, the effects of **toluene** diisocyanate on rat trachea ring and lung parenchymal strip were studied in vitro. The most prominent effect observed was a stimulation of metacholine induced contraction of the tracheal ring by 1M **toluene** diisocyanate (added in dimethyl sulfoxide). The results were less pronounced when **toluene** diisocyanate was added from a stock solution prepared in water, which is possibly due to copolymerisation. It is concluded that the pharmacological effect of **toluene** diisocyanate may result from an autonomic imbalance between cholinergic and B-adrenergic neural control.
[Borm PJA et al; Br J Ind Med 46 (1): 56-9 (1989)]**PEER REVIEWED**

Mechanism of Action :

SERUM FROM 26 PERSONS SHOWN TO REACT TO PROVOCATIVE INHALATION CHALLENGE WITH LOW CONCN OF **TOLUENE** DIISOCYANATE WAS TESTED BY RADIOALLERGOSORBENT TEST (RAST) USING A P-TOLYL ISOCYANATE-HUMAN SERUM ALBUMIN (TMI-HSA) CONJUGATE. POSITIVE RESULTS WERE OBTAINED IN 15-19% OF **TOLUENE** DIISOCYANATE REACTORS, DEPENDING ON THE METHOD OF EVALUTION. **TOLUENE** DIISOCYANATE ASTHMA MAY BE A COMPLEX SYNDROME WITH SEVERAL TYPES OF REACTIONS POSSIBLE, INCLUDING AN IMMUNOGLOBULIN-E MECHANISM IN SOME INDIVIDUALS. THE THEORY THAT **TOLUENE** DIISOCYANATE ASTHMA IS BASED SOLELY ON AN IMMUNE MECHANISM IS NOT SUPPORTED. THE FINDINGS DO NOT DISAGREE WITH THE HYPOTHESIS THAT **TOLUENE** DIISOCYANATE REACTIVITY MAY BE MEDIATED BY A PHARMACOLOGIC MECHANISM.
[BUTCHER BT ET AL; J ALLERGY CLIN IMMUNOL 66 (3): 213 (1980)]**PEER REVIEWED**

Mechanism of Action :

Intravenously administered endotoxin inhibits the polymorphonuclear leukocyte dependent airway edema produced in guinea pigs exposed to **toluene** diisocyanate. Tumor necrosis factor is produced in vivo by peripheral blood monocytes and tissue macrophages stimulated with endotoxin and has been shown to activate polymorphonuclear leukocyte's and vascular endothelial cells. To determine whether the inhibition of airway edema is mediated by tumor necrosis factor, guinea pigs were treated with intravenous saline or 75,000 U/kg recombinant human tumor necrosis factor 1.5 hr before exposure to air or 3 ppm **toluene** diisocyanate for 1 hr. Animals were then injected intravenously with 50 mg/kg Evans blue dye as a marker of protein extravasation. Saline-treated animals exposed to **toluene** diisocyanate had a significant increase in tracheal Evans blue dye extravasation (85 + or - 6.5 ug dye/g trachea, mean + or - standard error) compared with saline-treated animals exposed to air (31.3 + or - 2.5, $P < 0.001$). The tracheal extravasation of Evans blue dye was significantly inhibited ($P < 0.05$) in **toluene** diisocyanate exposed animals treated with tumor necrosis factor (64.7 + or - 7.5). Neither heat-inactivated tumor necrosis factor (104.9 + or - 9.5) nor tumor necrosis factor neutralized with a monoclonal antibody against tumor necrosis factor (99.7 + or - 17.9) inhibited **toluene** diisocyanate induced airway edema. In addition, treatment with 15,000 U/kg (99.9 + or - 21.3) or 150,000 U/kg (103.2 + or - 17.6) interleukin 1, a monokine also produced in response to endotoxin, did not prevent airway edema. These results suggest that tumor necrosis factor released in response to endotoxin mediates endotoxin's inhibition of a polymorphonuclear leukocyte dependent airway edema.
[Gordon T, Sheppard D; J Appl Physiol 64 (4): 1988 1688-92]**PEER REVIEWED**

Mechanism of Action :

Light and electron microscopic structure of lobar bronchial biopsies were examined of nine subjects with occupational asthma induced by **toluene** diisocyanate and of four control nonasthmatic subjects who had never been exposed to **toluene** diisocyanate. Inflammatory cell

numbers were separately assessed in the intact epithelium, in the more superficial layer of the submucosa, and in the total submucosa. Asthmatic subjects had an increased number of inflammatory cells in the airway mucosa compared with control subjects. Eosinophils were significantly increased in all compartments, CD45-positive cells were significantly increased in the epithelium and in the more superficial layer of the submucosa, and mast cells were significantly increased only in epithelium. By electron microscopy eosinophils and mast cells appeare degranulated only in asthmatic patients. In the areas of epithelium that appeared intact by light microscopy, electron microscopy showed that, although the intercellular spaces between columnar cells were similar in asthmatic and control groups, the intercellular spaces between basal cells were significantly wider in patients with asthma. Patients with **toluene** diisocyanate induced asthma also had a thicker subepithelial reticular layer, where immunohistochemistry showed the presence of collagen III. In conclusion, in patients with asthma induced by **toluene** diisocyanate, the airway mucosa shows pathologic features, such as inflammatory cell infiltrate and thickening of subepithelial collagen, similar to those described in atopic asthma.
[Saetta M et al; Am Rev Respir Dis 145 (1): 160-8 (1992)]**PEER REVIEWED**

Probable Routes of Human Exposure :

In a Finnish study, TDI vapor concentrations ranged from 25-80 ug/cu m for pouring, 14-44 ug/cu m for paper stripping, and 1-8 ug/cu m for cutting(1). Personal monitors measured 9-34 ug/cu m and 5-30 ug/cu m of the 2,4-isomer for pouring and paper stripping, respectively(1). While 2,4-**toluene** diisocyanate constitutes 80% of TDI, and 2,6-**toluene** diisocyanate 20%, the 2,4-isomer is more reactive so that the concentration of the 2,6-isomer is higher in workplace air(1). The percentage of 2,4-**toluene** diisocyanate to total **toluene** diisocyanate measured with the personal monitors ranged from 29 to 69%(1). TDI levels of 1.3-2.8 ppb were detected in air inside a Swedish factory manufacturing polyurethanes(2).
[(1) Rosenberg C, Savolainen H; J Chromatography 367: 385-92 (1986) (2) Audunsson G et al; Intern J Environ Anal Chem 20: 85-100 (1985)]**PEER REVIEWED**

Analytic Laboratory Methods :

A passive monitor for **toluene** diisocyanate which utilizes microporous Teflon diffusion membranes and a 0.5% sulfuric acid absorbing medium was evaluated. The collection rate of **toluene** diisocyanate is proportional to exposure dose from 10 to at least 300 ppb.hr, and response is equivalent for 2,4- and 2,6-**toluene** diisocyanate. Collection rate is independent of humidity and normal atmospheric pressure variations, while temperature causes a decrease of 1.0% per deg C. Negative interference caused by ambient nitrogen dioxide is eliminated by addition of sulfamic acid to the collecting medium. N-Ethylmorpholine is a positive interferent. Field testing of the sampler against a reference impinger technique indicated a positive bias when **toluene** diisocyanate is aerosolized.
[Rando RJ et al; Am Ind Hyg Assoc J 50 (1): 8-14 (1989)]**PEER REVIEWED**

Environmental Fate/Exposure Summary :

Commercial **toluene** diisocyanate (TDI) is composed of 2 isomers. 2,4-**Toluene** diisocyanate constitutes roughly 80% of TDI, the other 20% being the 2,6-isomer. It may be released to the environment as fugitive emissions and from stack exhaust during the production, transport, and use of TDI in the manufacture of polyurethane foam products and coatings as well as from spills. The types of reactions which the isomers undergo are similar, although the rates may differ. The reactivity of the 2,4-**toluene** diisocyanate with active hydrogen is greater than with the 2,6-isomer, therefore the percentage of 2,4-**toluene** diisocyanate in monitored TDI is generally much less than the 80% in the commercial mixture. However, since much of the monitoring data do not distinguish between isomers, it is not possible to know the proportion of the isomers in the TDI. If spilled on wet land, TDI is rapidly degraded. In one experiment simulating a spill, 5.5% of the original material remained after 24 hours and in a field situation, the concentration of TDI had declined to the ppm levels in 12 weeks. If released into water, a crust forms around the liquid TDI and <0.5% of the original material remains after 35 days. Low concentrations of TDI disappear from the aqueous environment in approximately a day. In

the atmosphere, TDI reacts with photochemically produced hydroxyl radicals (half-life 3.3 hr) and is also removed by dry deposition. Human exposure is primarily occupational via inhalation and dermal contact. (SRC)
PEER REVIEWED

Human Toxicity Excerpts :

A survey of the incidence of occupational asthma in a steel coating factory was conducted. The survey was prompted by two male employees developing symptoms suggestive of occupational asthma. The cohort consisted of 221 males employed in the coating shop. A respiratory questionnaire was administered. Spirometric tests were conducted. Peak expiratory flow rate studies were performed on 50 subjects. Twenty one subjects reported symptoms of occupational asthma. Sixty three had other work related symptoms and 58 had respiratory symptoms unrelated to work. The mean length of employment of the subjects with asthmatic symptoms was 7.7 years. All symptomatic subjects had significantly reduced 1 second forced expiratory volumes, compared to asymptomatic workers. 21% of the peak expiratory flow rates were indicative of work related asthma. Two symptomatic subjects were administered inhalation challenge tests with **toluene** diisocyanate after it was discovered that one of the coatings that had been used for 8 years released **toluene** diisocyanate during the coating process. Both subjects showed decreases in forced expiratory volumes of at least 15% below the baseline values. Environmental sampling for **toluene** diisocyanate indicated concentrations ranging from below 0.001 to 0.026 ppm. The coating containing **toluene** diisocyanate was removed from the process. A follow-up survey conducted 1 year later showed that 17 of the symptomatic subjects had become asymptomatic or improved.
[Venables KM et al; Brit J Indus Med 42 (8): 517-24 (1985)]**PEER REVIEWED**

Human Toxicity Excerpts :

The prevention of airway inflammation caused by **toluene** diisocyanate by prednisone was studied. Healthy **toluene** diisocyanate sensitive individuals were exposed to 0.018 ppm **toluene** diisocyanate in a test chamber. Bronchoalveolar lavage fluid was collected with a flexible fiberoptic bronchoscope. The lavage fluid was spun in a cytocentrifuge and stained with May/Grunwald/Giemsa for differential cell count. The total cell count was performed on resuspended cell pellets. A late asthmatic response was characterized by the occurrence of less than 20% of free expiratory volume in 1 second. The airway responsiveness was assessed by the reaction to methacholine. The cumulative dose of methacholine that produced a 20% decrease in forced expiratory volume in 1 second was used to measure airway responsiveness. Five subjects who received no prednisone treatment developed a late or dual asthmatic reaction. The albumin concn and total number of cells increased in subjects that were given no prednisone compared to controls. There was a significant increase in the number of neutrophils and a small increase in eosinophilia. There was no significant difference in the counts of other cell types. Results suggest that **toluene** diisocyanate induce late asthmatic reactions causing airway inflammation and that prednisone inhibits these reactions.
[Boschetto P et al; J Allergy Clin Immunol 80 (3):261-267 (1987)]**PEER REVIEWED**

Metabolism/Metabolites :

Epithelial injury and inflammation are involved in airway hyperresponsiveness and asthma induced by **toluene** diisocyanate. In that isocyanates are insoluble and highly reactive compounds, bronchial epithelial cells may represent the most important target cells of their toxic effect. We hypothesized that damage to airway epithelium by **toluene** diisocyanate may result in the release of metabolites of arachidonic acid, which are known to promote inflammation and to alter epithelial cell function and airway smooth muscle responsiveness. To test this hypothesis we examined eicosanoid products in the culture media of bronchial epithelial cells exposed in vitro to 8 and 18 ppb **toluene** diisocyanate. Epithelial cells derived from human bronchi obtained at surgery were cultured to confluency on collagen-coated microporous membranes. Those cells, which expressed differentiated characteristics of epithelial cells (they showed keratin-containing filaments and had a cobblestone appearance), were alternatively exposed to **toluene** diisocyanate or air for 30 min in a specially designed in vitro chamber. The production of metabolites of arachidonic acid was assessed by measuring the release of immunoreactive

products into the cell medium at the end of the exposure and during a 2 hr period after exposure. This method revealed a predominant isocyanate induced release of immunoreactive 15-hydroxyeicosatetraenoic acid. Release rate of this compound tended to be dose-related and was associated with cell damage as assessed by the release of lactate dehydrogenase in the medium.
[Mattoli S et al; J Cell Physiol 142 (2): 379-85 (1990)]**PEER REVIEWED**

Emergency Medical Treatment :

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The following Overview, *** **TOLUENE** DIISOCYANATE ***, is relevant for this HSDB record chemical.

Life Support:

- This overview assumes that basic life support measures have been instituted.

Clinical Effects:

SUMMARY OF EXPOSURE

0.2.1.1 ACUTE EXPOSURE

- **Toluene** diisocyanate is an irritant to skin, lungs, conjunctiva and gastrointestinal tract. Euphoria, ataxia, mental aberrations, sensitization (primarily respiratory), bronchitis, emphysema and cor pulmonale can occur.

HEENT

0.2.4.1 ACUTE EXPOSURE

- Severe conjunctival irritation and lacrimation from liquid or high vapor concentrations is likely. Lower concentrations may produce a burning or prickling sensation.
- Glaucoma and iridocyclitis have been reported with a splash accident.

RESPIRATORY

0.2.6.1 ACUTE EXPOSURE

- Burning or irritation of the nose and throat, cough, laryngitis, chest pain, and asthmatic syndrome (chemical bronchitis with severe bronchospasm), sensation of oppression or constriction of the chest, bronchitis, emphysema and cor pulmonale may occur.
- Respiratory symptoms may recur several years after discontinuation of exposure.

NEUROLOGIC

0.2.7.1 ACUTE EXPOSURE

- Acute exposures may produce headache, insomnia, euphoria, ataxia, anxiety neurosis with depression, or paranoid tendencies.

GASTROINTESTINAL

0.2.8.1 ACUTE EXPOSURE

- Inhalation of vapor or aerosol may produce vomiting and abdominal pain. Epigastric and substernal pain may be secondary to the paroxysmal or persistent cough

associated with inhalation.

DERMATOLOGIC

0.2.14.1 ACUTE EXPOSURE

- Irritation and inflammation are common. Dermal absorption is low.

IMMUNOLOGIC

0.2.19.1 ACUTE EXPOSURE

- Elevated specific IgE and IgG antibodies have been detected in sensitized and exposed workers. The presence of antibodies does is an indicator of exposure but not of sensitization.

CARCINOGENICITY

0.2.21.1 IARC CATEGORY

- **Toluene** diisocynate has been classified as a 2B agent: possibly carcinogenic to humans, based on sufficient evidence of carcinogenicity in experimental animals and no human data (IARC, 1987).

0.2.21.2 HUMAN OVERVIEW

- **Toluene** diisocyanate is considered a suspected or possible human carcinogen, based on sufficient evidence of carcinogenicity or tumors (spleen, subcutaneous, hepatic, ovarian, peritoneum, mammary gland tissues) in experimental animals (IARC, 1987; US DHHS, 1994; ACGIH, 1995).

Laboratory:

- Monitor respiratory function closely.

Treatment Overview:

ORAL EXPOSURE

- Due to the irritant nature of this substance, emesis is not advised.
- DILUTION: Immediately dilute with 4 to 8 ounces (120 to 240 mL) of milk or water (not to exceed 15 mL/kg in a child).
- ACTIVATED CHARCOAL: Administer charcoal as slurry (240 mL water/30 g charcoal). Usual dose: 25 to 100 g in adults/adolescents, 25 to 50 g in children (1 to 12 years), and 1 g/kg in infants less than 1 year old.
- Monitor patient for respiratory distress. If a cough or difficulty in breathing develops, evaluate for respiratory tract irritation, bronchitis and pneumonia.
- Allergic reaction: Sensitized individuals should be cautioned to avoid further exposure as serious allergic reactions may result.

INHALATION EXPOSURE

- DECONTAMINATION: Move patient to fresh air. Monitor for respiratory distress. If cough or difficulty in breathing develops, evaluate for respiratory tract irritation, bronchitis, or pneumonitis. Administer 100 percent humidified supplemental oxygen with assisted ventilation as required.
- Randomized, double-blind cross-over studies showed minimal efficacy of bronchodilators. This could be due to the absence of airway hyperresponsiveness in some TDI-induced asthma.

EYE EXPOSURE

- DECONTAMINATION: Exposed eyes should be irrigated with copious amounts of tepid water for at least 15 minutes.

If irritation, pain, swelling, lacrimation, or photophobia persist, the patient should be seen in a health care facility.

DERMAL EXPOSURE

- DECONTAMINATION: Wash exposed area extremely thoroughly with soap and water. A physician may need to examine the area if irritation or pain persists.

Range of Toxicity:

- Available dose-response information concerning humans pertains to inhalational exposure. Concentrations of 2.5 ppm are considered Immediately Dangerous to Life or Health. A fatality in an asthmatic who continued exposure to TDI has been reported.
- The recommended short term exposure limits for TDI in industry is 0.02 ppm. TDI does not have sufficient warning properties (e.g. odor or eye irritancy) at air concentrations below the recommended short term exposure limit.

[Rumack BH: POISINDEX(R) Information System. Micromedex, Inc., Englewood, CO, 2001; CCIS Volume 107, edition exp February, 2001. Hall AH & Rumack BH (Eds):TOMES(R) Information System. Micromedex, Inc., Englewood, CO, 2001; CCIS Volume 107, edition exp February, 2001.] **PEER REVIEWED**

National Toxicology Program Studies :

Groups of 50 female F344/N rats and 50 female B6C3F1 mice were administered commercial grade **toluene** diisocyanate (80% 2,4- and 20% 2,6-) in corn oil by gavage at doses of 60 or 120 mg/kg body weight, 5 days per week for 105 or 106 weeks. Groups of 50 male F344/N rats received 30 or 60 mg/kg and groups of 50 male B6C3F1 mice received 120 or 240 mg/kg on the same schedule. Dosage analyses of **toluene** diisocyanate indicated that the chemical had reacted in the corn oil vehicle, resulting in actual gavage concentrations 77% to 90% of theoretical values. Groups of 50 rats and 50 mice of each sex received corn oil only and served as vehicle controls. Survival in all groups of dosed rats in the 2-year studies was shorter (P less than or equal to 0.005) than that of the controls; depressions in mean body weight gain relative to controls were greater than 10% in all dosed rat groups throughout most of the study. A dose-dependent pattern of cumulative toxicity began at 70 weeks and culminated in excessive mortality, indicating the estimated maximum tolerated dose had been exceeded for rats. Acute bronchopneumonia occurred at increased incidences in groups of dosed male and female rats (males: control, 2/50; low dose, 6/50; high dose, 14/50; females: 1/50, 10/50, 25/49). /Results indicated that/ commercial grade **toluene** diisocyanate in corn oil was carcinogenic for F344/N rats, causing subcutaneous fibromas and fibrosarcomas (combined) in males and females, pancreatic acinar cell adenomas in males, and pancreatic islet cell adenomas, neoplastic nodules of the liver, and mammary gland fibroadenomas in females. **Toluene** diisocyanate was not carcinogenic for male B6C3F1 mice. TDI was carcinogenic for female B6C3F1 mice, causing hemangiomas or hemangiosarcomas (combined), as well as hepatocellular adenomas.
[DHHS/NTP; Toxicology and Carcinogenesis Studies of Commercial Grade 2,4 (80%) and 2,6 (20%) - Toluene Diisocyanate (Gavage Studies) p. 7 (1986) Technical Rpt Series No. 251 NIH Pub No. 86-2507]**PEER REVIEWED**

Human Toxicity Excerpts :

The importance of airways inflammation for the development of bronchial hyperresponsiveness and for exacerbation of asthma was investigated in subjects with occupational asthma. Subjects sensitized to isocyanates, a small molecular weight compound that causes occupational asthma were examined. Studies in asthmatic subjects sensitized to **toluene** diisocyanate demonstrated that late, but not early, asthmatic reactions induced by **toluene** diisocyanate were associated

with an acute increase in bronchial responsiveness, and with a marked infiltration of neutrophils and a slight infiltration of eosinophils into the airways, both prevented by steroids. As the late asthmatic reactions and the increase in responsiveness induced by **toluene** diisocyanate were prevented by steroids, but not by indomethacin, it was speculated that cell membrane phospholipid metabolites, which are inhibited by steroids but not by indomethacin, may be involved in **toluene** diisocyanate induced hyperresponsiveness. The results of these studies suggest that bronchial hyperresponsiveness and exacerbation of asthma may be related to inflammation of the airways and that cell membrane phospholipid metabolites may be involved.
[Mapp CE et al; Bull Eur Physiopathol Respir 23 (6): 583-6 (1987)]**PEER REVIEWED**

Human Toxicity Excerpts :

Fifty seven polyurethane foam manufacturing workers and 24 reference workers were followed for 4 yr to clarify the effects on pulmonary function of working in polyurethane foam factories with exposure to **toluene** diisocyanate. No significant differences in the average annual losses of pulmonary function for 4 yr were observed among the 28 polyurethane foam workers whose **toluene** diisocyanate exposure levels were very low (mean = 0.1 ppb, group L), the remaining 29 polyurethane foam workers with mean **toluene** diisocyanate exposure of 5.7 ppb (group H), and the reference workers. However, 15 polyurethane foam workers in group H who had experienced peak exposure excursions to 30 ppb or above with a mean concn of 8.2 ppb showed significantly larger average annual losses in percentage maximal mid-expiratory flow, forced expiratory volume in 1 sec ratio to vital capacity, and forced expiratory flow at 25% of forced vital capacity than expected, and significantly larger average annual losses in some obstructive pulmonary function indices than those of the 14 remaining polyurethane foam workers in group H whose peak exposure excursion levels were 3-14 ppb with a mean time-weighted average of 1.7 ppb, group L, and the reference workers. These findings suggest that the peak exposure excursion level of **toluene** diisocyanate might be important in inducing obstructive pulmonary function changes in the polyurethane foam workers rather than the TWA exposure levels, though further comparative studies of the AAL in those who are exposed to different peak exposure excursion levels but the same mean exposure levels are necessary. From the standpoint of prevention, the proposition that peak exposure excursion levels exceeding 20 ppb should be avoided is reasonable.
[Omae K et al; Int Arch Occup Environ Health 63 (8): 565-9 (1992)]**PEER REVIEWED**

Human Toxicity Excerpts :

The clinical findings and the results of inhalation challenge with **toluene** diisocyanate and methacholine in 113 subjects with a history of exposure to **toluene** diisocyanate and work-related respiratory symptoms are reported. Only some of the subjects (40.7%) had isocyanate asthma, diagnosed by a positive **toluene** diisocyanate inhalation challenge. Most reactors had a dual (30.4%) or a late (41.3%) response. The interval between the last occupational exposure and the specific challenge was significantly shorter in reactors, and among this group the number of immediate reactions to **toluene** diisocyanate decr progressively with an incr interval. The reactors had a significantly higher proportion of positive responses to methacholine and a significantly lower mean PD[1][5] FEV[1] (provocative dose of methacholine which provoked a 15% decrease in forced expiratory volume in 1 second): reactors 557:g, SEM 92.3; non-reactors 1346:g, SEM 128, P < .01. Methacholine challenge could not identify subjects with isocyanate asthma.
[Moscato G et al; J Occup Med 33 (6): 720-5 (1991)]**PEER REVIEWED**

Human Toxicity Excerpts :

To evaluate the morphologic basis of the different outcomes of **toluene** diisocyanate asthma after quitting occupational exposure, ten patients with **toluene** diisocyanate asthma were examined who showed, at diagnosis, a positive **toluene** diisocyanate challenge test and nonspecific bronchial hyperresponsiveness to methacholine. After diagnosis, all patients ceased work and a 4 to 40 mo follow-up was obtained with three to eight determinations of the cumulative dose producing a 15% fall in forced expiratory volume in 1 second to methacholine in each patient. Bronchoalveolar lavage and biopsy of bronchial muscosa were performed 3 to

39 mo after cessation of work, in the absence of acute exacerbations of the disease. Total cell count in bronchoalveolar lavage fluid was moderately increased in four of ten patients, eosinophils were increased in five of ten patients, and neutrophils were increased in eight of ten patients. Mucosal biopsy specimens of main or lobar bronchi were available in eight of ten patients; epithelial damage and thickening of basement membrane was observed in almost all patients, as well as a mild to moderate inflammatory reaction in the submucosa, mainly represented by lymphocytes, eosinophils, and neutrophils. No relationship was observed between the cellularity of bronchoalveolar lavage and the degree of nonspecific bronchial hyperresponsiveness at the time of bronchoalveolar lavage; mean values of total cells and differential count were not different between patients with presence or absence of the different histologic findings. Mucosal biopsy and bronchoalveolar lavage were performed also in four subjects exposed to dusts without respiratory symptoms or nonspecific bronchial hyperresponsiveness; similar findings were obtained except for the absence of eosinophils in bronchoalveolar lavage and a lesser degree of basement membrane thickening and inflammatory reaction in the submucosa. The study of the changes in nonspecific bronchial hyperresponsiveness after quitting exposure showed that five of ten patients had a significant improvement in nonspecific bronchial hyperresponsiveness to methacholine, as evaluated by a positive significant linear regression between months of work cessation and forced expiratory volume in 1 sec of methacholine; only one of these five patients had an increased number of eosinophils in bronchoalveolar lavage fluid. By contrast, four of the five patients with persistent nonspecific bronchial hyperresponsiveness after quitting exposure had an increased number of eosinophil in bronchoalveolar lavage. It is suggested that persistent nonspecific bronchial hyperresponsiveness in **toluene** diisocyanate asthma after cessation of work may be related to an inflammatory reaction in which eosinophil infiltration seems to be a major determinant.
[Paggiaro P et al; Chest 98 (3): 536-42 (1990)]**PEER REVIEWED**

Human Toxicity Excerpts :

A 41 yr old automobile paint sprayer showed the clinical features of hypersensitivity pneumonitis 1 wk after he had begun to work with paint materials containing **toluene** diisocyanate. His symptoms began 6 to 8 hr after exposure to the agent and spontaneously disappeared by the next morning. He had diffuse, fine reticulonodular shadows on a chest roentgenogram and a restrictive impairment of pulmonary function. Immunoglobulin G antibody to **toluene** diisocyanate-human serum albumin was present in bronchoalveolar lavage fluid and sera: IgA antibody was present only in bronchoalveolar lavage fluid. Also, the patient had sensitized bronchoalveolar lymphocytes to **toluene** diisocyanate-human serum albumin. The histologic findings suggested hypersensitivity pneumonitis. The results of bronchoalveolar lavage, which was repeated on four separate occasions, showed lymphocytosis and a predominance of suppressor cytotoxic T cells. The findings from serial determinations of humoral antibodies showed no changes consistent with the results of clinical and laboratory studies. In contrast, blastogenic responses of bronchoalveolar lymphocytes to **toluene** diisocyanate markedly decr, and the patient showed clinical improvement despite continued exposure to the agent.
[Yoshizawa Y et al; Ann Intern Med 110 (1): 31-4 (1989)]**PEER REVIEWED**

Human Toxicity Excerpts :

A case of building related health complaints was investigated with respect to the relationship among frequency of symptoms, antibodies to albumin conjugates of formaldehyde, **toluene** diisocyanate, and trimellitic anhydride, and volatile organic chemicals. The indoor air concn of volatile organic chemicals, formaldehyde, **toluene** diisocyanate and trimellitic anhydride did not exceed Fed-OSHA and ACGIH permissible standards. However, formaldehyde concn ranged between 0.05 and 0.08 ppm. The reported symptoms were multiple, involving the eyes, nose, sinuses, throat, lungs, skeletomuscular system and central nervous system. Anti-formaldehyde, **toluene** diisocyanate, and trimellitic anhydride isotypes were found in 12 of 14 full-time employees and were nondetectable in one part-time employee. The data suggest that a synergistic immunological response to airborne chemicals may be occurring in these subjects. In conclusion, immunological monitoring of affected individuals where chemicals are suspected may prove to be useful in future investigations of building related illness.
[Thrasher JD et al; Am J Ind Med 15 (2): 187-95 (1989)]**PEER

REVIEWED**

Mechanism of Action :

The in vivo exposure to an asthmogenic stimulus, **toluene** diisocyanate, causes airway epithelial damage associated with inflammation and increased bronchial hyperresponsiveness. The latter mechanisms might partly be mediated by the release of eicosanoids from bronchial epithelial cells. Previously it has been demonstrated that the in vitro exposure of bronchial epithelial cells to **toluene** diisocyanate results in the release of immunoreactive 15-hydroxyeicosatetraenoic acid, a product of activation of the 15-lipoxygenase pathway with inflammatory properties. Present study shows that **toluene** diisocyanate induced release of 15-hydroxyeicosatetraenoic acid from epithelial cells can be prevented by nedocromil sodium, an anti-asthmatic drug with anti-inflammatory properties. This mode of action of the compound may explain its clinical effectiveness in asthma.
[Mattoli S et al; Int Arch Allergy Appl Immunol 92 (1): 16-22 (1990)]**PEER REVIEWED**

Human Toxicity Excerpts :

Thirty factory workers whose annual exposure to **toluene** diisocyanate amounted to 280 hr were examined. Seven of them had been removed from their jobs for presenting respiratory symptomatology and a further five were removed for presenting bronchial asthma. Their medical histories were consulted and further measures were taken such as a radiological thorax study, total immunoglobulin-E, **toluene** diisocyanate, diphenylmethane diisocyanate and hexamethylene diisocyanate RAST, a basal spirometric study and finally a provocation test. The Rast proved negative in every case. In the spirometric study carried out on the provocation test, four cases showed a significant decrease in the forced expiratory volume in 1 second over 20% and over 40% in the FMEF and PEFR. There was no connection between the four patients who presented an elevated total immunoglobulin-E and the four who presented a positive provocation test. The provocation test proved negative in five of the seven patients removed from their places of work. Two of the four workers who responded positively to the provocation test remained in their places of work during the **toluene** diisocyanate foam test without showing any symptoms. The patients who presented symptoms did not appear to present bronchial obstruction during the provocation test. Nonetheless, patients who seemingly had not shown any symptoms presented what appeared to be bronchial obstruction.
[Duce F et al; Allergol Immunopathol (Madr) 16 (3): 139-44 (1988)]**PEER REVIEWED**

Major Uses :

POLYURETHANE ELASTOMERS MADE FROM **TOLUENE** DIISOCYANATES ARE USED IN COATED FABRICS & CLAY-PIPE SEALS. **TOLUENE** DIISOCYANATES ARE ALSO USED IN ADHESIVES OF POLYURETHANE & OTHER TYPES. /**TOLUENE** DIISOCYANATES/
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V19 307 (1979)]**PEER REVIEWED**

Non-Human Toxicity Excerpts :

In dogs, a correlation has been made between immunological and respiratory responses to **toluene** diisocyanate. Dogs exposed once every second week for 41 wk to 1 mg/kg **toluene** diisocyanate delivered as an aerosol intratracheally developed a systemic immune response to **toluene** diisocyanate conjugated with dog serum albumin as well as immediate-type airway responses.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 307 (1986)]**PEER REVIEWED**

Human Toxicity Excerpts :

A series of workers with exposure to and respiratory symptoms from **toluene** diisocyanate was compared with a group of exposed, asymptomatic workers and with normal controls using immunologic and clinical evaluations. Improved understanding of **toluene** diisocyanate-induced respiratory disease may best be achieved by categorizing the symptomatic workers into at least 3 and possibly 4 groups: immunologic asthma; pre-existing chronic respiratory disease exacerbated or unaffected by **toluene** diisocyanate; asthma coincidental with exposure, and possibly respiratory disease secondary to toxic or inflammatory mechanisms.
[Patterson R et al; Int Arch Allergy Appl Immunol 84 (1): 93-100 (1987)]**PEER REVIEWED**

Sediment/Soil Concentrations :

Ten days after an accident resulting in the spillage of 13 tons of **toluene** diisocyanate from a lorry on a swampy wet forest area, **toluene** diisocyanate and toluenediamine were /found/ in the soil. After six yr, only **toluene** diisocyanate-derived polyureas were found in soil samples taken at the same site.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 299 (1986)]**PEER REVIEWED**

Human Toxicity Excerpts :

The nature of neurohumoral regulation was studied in 125 healthy workers, aged 20-40 yr, with different length of service and **toluene** diisocyanate exposure levels. Adrenal gland activity and some haematological parameters were determined. Neurohumoral regulation of adaptation processes in **toluene** diisocyanate exposed persons seemed to display some cyclicity, somehow related to the length of service. Two early regulatory phases (service up to 3 yr) had common features unrelated to the exposure levels, while after 3 yr of employment some dissimilarities evolved which did depend on the **toluene** diisocyanate exposure levels.
[Ermakova GA, Kryzanovskaja NA; Gigiena truda i Professional'nye Zabolevanija (7): 22-35 (1988)]**PEER REVIEWED**

NIOSH Recommendations :

Experimental studies have demonstrated that **toluene** and TDA (a hydrolysis product of **toluene** diisocyanate) are carcinogens. The test results meet both OSHA and NIOSH criteria for classifying a substance as a potential occupational carcinogen. NIOSH therefore recommends that all isomers of **toluene** diisocyanate and TDA be considered as potential carcinogens and that exposures be limited to the lowest feasible concn.
[ANON; USDHHS, Public Health Service, Centers for Disease Control, NIOSH, Division of Standards Development and Technology Transfer, 4676 Columbia Parkway, Cincinnati OH 45226, USA, 1989. 20p. Bibl.]**PEER REVIEWED**

Sampling Procedures :

NIOSH Method: 5521. Analyte: 2,6-**Toluene** diisocyanate. Matrix: Air. Sampler: Impinger (solution of 1-(2-methoxyphenyl)-piperazine in **toluene**). Flow Rate: 1 l/min. Sample Size: 100 liters. Shipment: Ship in screw-cap vial refrigerated @ 4 deg C or lower. Sample Stability: May be unstable; perform steps 8 and 9 as soon as possible. /2,6-**Toluene** diisocyanate/
[U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. 5521-1]**PEER REVIEWED**

Human Toxicity Excerpts :

Toluene diisocyanate is commonly used as the 2,4 and 2,6 isomers. NIOSH has estimated that 50,000 to 100,000 workers in the United States are regularly exposed to diisocyanates. As of 1977, 49,996 were estimated to be exposed to **toluene** diisocyanate alone. Methods for

measuring diisocyanate exposures were considered. The current American Conference of Governmental Industrial Hygienists' recommended standard is 0.005 ppm time weighted average and 0.02 ppm peak for four 15 min periods a day. Results of exposure measurements taken in industry were summarized. Health effects of diisocyanates were discussed. In laboratory animals, **toluene** diisocyanate has caused inflammation and necrosis when applied directly to the skin, conjunctivitis when applied to the eyes, and rhinitis, laryngitis, tracheitis, bronchitis, and pneumonia when inhaled. Diisocyanates are potent pulmonary sensitizers capable of causing isocyanate asthma in humans. They can induce nonspecific airways disease and hypersensitivity pneumonitis after either acute or chronic exposure.
[Musk AW et al; Am J Ind Med 13 (3): 331-49 (1988)]**PEER REVIEWED**

Human Toxicity Excerpts :

A 46 yr old man who had worked in a paint processing plast for over 29 yr was admitted to our hospital with complaints of nocturnal dyspnea and dry cough. A chest X-ray film showed diffuse granular shadows in bilateral lungs. Pulmonary function tests revealed reduction of diffusing capacity and restrictive impairments. Hypersensitivity pneumonitis due to isocyanates was speculated from his occupational history and clinical course. Positive skin tests against **toluene** diisocyanate-human serum albumin and diphenylmethane diisocyanate-human serum albumin, precipitating antibody against **toluene** diisocyanate-human serum albumin, and negative lymphocyte stimulating tests of peripheral blood and bronchoalveolar lavage fluid were also noticed. Environmental provocation test was positive. Histological findings of transbronchial lung biopsy specimens showed diffuse alveolitis and Masson body, but no granulomas. According to these results, the patient was diagnosed as hypersensitivity pneumonitis due to **toluene** diisocyanate. Type III allergy of Gell-Coombs seems to participate in this case. The granulomatous lesion is seen less frequently in isocyanate related hypersensitivity pneumonitis than in hypersensitivity pneumonitis induced by organic dusts, which suggests the difference in immunological and histological reactions between both types of hypersensitivity pneumonitis.
[Nozawa S et al; Nippon Kyobu Shikkan Gakkai Zasshi 27 (11): 1335-41 (1989)]**PEER REVIEWED**

Analytic Laboratory Methods :

NIOSH Method: 5521. Analyte: 2,6-**Toluene** diisocyanate. Matrix: Air. Procedure: High performance liquid chromatography, electrochemical and ultra violet detection. For 2,6-**toluene** diisocyanate this method has an estimated detection limit of ca. 0.1 ug diisocyanate/sample. The precision/RSD is not determined and the recovery is not given. Applicability: The working reange is from ug/cu m to more than 1 mg/cu m for a 100 liter air samples. Interferences: Any cmpd which elutes with ureas and absorbs ultraviolet light or is electroactive will interfere with the analysis. /2,6-**Toluene** diisocyanate/
[U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. 5521-1]**PEER REVIEWED**

Mechanism of Action :

Inhalation of **toluene** diisocyanate results in toxic responses ranging from pulmonary irritation to immunological sensitization. The use of radioactively labeled isocyanate has made it possible to follow the initial uptake of the compound into the bloodstream independent of the final fate of the isocyanate. This study shows that the rate of uptake into the blood is linear during exposure to concn ranging from 0.00005 to 0.146 ppm and that the uptake continues to increase slightly postexposure. It also demonstrates that the radioactivity clears from the bloodstream to a level corresponding to approximately a 100 nM concn of tolyl group after 72 hr and persists at a nanomolar level even 2 wk following the exposure. The initial rate of (14)C uptake is also a linear function of the concn of **toluene** diisocyanate when expressed either as concn (ppm) or as concn multiplied by duration of exposure (ppm.hr). This is discussed in comparison with the toxic responses as a function of both ppm and ppm.hr. Finally, the inclusion of the data on

methyl isocyanate indicates that the uptake into arterial blood is a function of exposure concn, independent of isocyanate structure.
[Kennedy AL et al; Toxicol Appl Pharmacol 100 (2): 280-92 (1989)]**PEER REVIEWED**

Immediately Dangerous to Life or Health :

NIOSH considers 2,4-**toluene** diisocyanate to be a potential occupational carcinogen. /2,4-**Toluene** diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

NIOSH Recommendations :

NIOSH considers 2,4-**toluene** diisocyanate to be a potential occupational carcinogen. /2,4-**Toluene** diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

Environmental Abiotic Degradation :

Toluene diisocyanate reacts readily with compounds containing active hydrogens, such as water, acids, and alcohols(2). Contact with bases may cause uncontrollable polymerization with rapid evolution of heat(2). In concentrated solutions, hydrolysis of one of the isocyanate groups to the amine is followed by rapid reaction of the amine with an isocyanate group on another molecule leading to dimers, oligimers, and polymers(2). In one experiment the hydrolysis product yield was 20% diamine and 80% polyurea(3). When 50 ppm of **toluene** diisocyanate was added to model river and seawater systems, the concn fell to 0.1 ppm or less at the end of 1 day(1).
[(1) Duff PB; The Fate of TDI in the Environment. In: Polyurethane-New Paths to Progress Marketing Technology. Proc. of the SPI 6th Inter. Tech. Marketing Conf. pp. 408-12 (1983) (2) IARC Monograph on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. 39: 287-323 (1985) (3) Sopach ED, Boltromeyuk LP; Gig Sanit 7: 10-3 (1974)]**PEER REVIEWED**

Sampling Procedures :

A solvent free sampling method for airborne **toluene** diisocyanate was described. Air samples were collected on quartz fiber filters impregnated with 1-(2-methoxyphenyl)piperazine. When the samples were collected on the 1-(2-methoxyphenyl)piperazine coated fibers, the collected **toluene** diisocyanate concn were not affected by changes in relative humidity.
[Robert A, Simon P; Chromatographia 23 (7):507-11 (1987)]**PEER REVIEWED**

Environmental Biodegradation :

Toluene diisocyanates are expected to be hydrolyzed much more rapidly than they are attacked by microorganisms. The resulting **toluene** diamines are subject to a wide variety of biochemical transformations.
[ITC/USEPA; Information Review #231 (Draft) Toluene Diisocyanates p. 19 (1981)]**PEER REVIEWED**

Mechanism of Action :

The beta-adrenoceptors on intact peripheral blood lymphocytes were studied in 21 allergic asthmatics, 11 **toluene** diisocyanate asthmatics and 17 normal subjects with radioligand binding assay technique. The airway responsiveness to methacholine provocation test was determined. The results indicated that beta-adrenoceptor Bmax values in allergic and **toluene** diisocyanate asthmatics were reduced but the affinity between receptor and ligand was increased; there was a positive correlation between the values of Bmax and forced expiratory volume in 1 second%, V25/Pr in both asthmatic groups, a positive correlation between the values of Bmax and PC20

in allergic asthmatics. The beta-adrenoceptor responsiveness was remarkably reduced in allergic asthmatics.
[Yang ZF et al; Chin J Tuberc Respir Dis 12 (3): 143-146, 190-191. (1989)]**PEER REVIEWED**

Non-Human Toxicity Excerpts :

GROUPS OF MALE & FEMALE RATS & MICE WERE EXPOSED TO 0.05 & 0.15 PPM OF 2,4/2,6-**TOLUENE**-DIISOCYANATE (80/20) BY INHALATION FOR 6 HR/DAY, 5 DAYS/WEEK FOR 2 YR. TYPE & INCIDENCE OF TUMORS & THE NUMBER OF TUMOR-BEARING ANIMALS OF EITHER SPECIES DID NOT INDICATE ANY CARCINOGENIC EFFECT. HEMATOLOGY, BIOCHEMISTRY, URINALYSIS, & CYTOGENICITY STUDIES DID NOT REVEAL ANY UNTOWARD EFFECT. INCREASED MORTALITY (FEMALES ONLY), REDUCED WEIGHT GAIN & SIGNS OF IRRITATION IN THE UPPER & LOWER RESPIRATORY TRACT RESULTED FROM EXPOSURE TO **TOLUENE** DIISOCYANATE IN THE MOUSE STUDY WITH THE HIGHEST INCIDENCE IN THE 0.15 PPM EXPOSURE LEVEL.
[LOESER E; TOXICOL LETT (AMST) 71 (1983)]**PEER REVIEWED**

Human Toxicity Excerpts :

The respiratory status of factory workers exposed continously to isocyanates over 10 years was studied. A total of 80 workers in two facilities that manufactured fixtures used in the interiors of cars were examined and underwent spirometry before and after work. Of these, 12 were comparisons not exposed to **toluene** diisocyanate. Subjects included those previously examined in 1971. Ventilatory capacity tests were performed inlcuding forced expiratory volume in 1 sec and forced vital capacity testing. Annual decrements were calculated. The mean average concentration of **toluene** diisocyanate was not more than 0.0033 ppm respectively. Subjects who had been studied previously had a mean forced vital capacity of 104.6% and a mean forced expiratory volume in 1 sec of 107% of predicted values. Three subjects with significant obstruction in the lung function tests were smokers. The comparisons in facility 1 had a significantly lower percentage of the predicted forced fital capacity and forced expiratory volume than the exposed population. Most of the data from 1971 for annual decrement calculations were not reliable. A 10% decrement in forced vital capacity and forced expiratory volume in 1 second was indicative of significant postshift decline and would indicate the presence of isocyanate asthma or hypersensitivity; no subject at either facility met the criteria.
[Gee JB; Morgan WKC; J Occup Med 27 (1): 15-8 (1985)]**PEER REVIEWED**

Human Toxicity Excerpts :

Amine induced asthma was studied in polyurethane foam workers. A total of 12 subjects, occupationally exposed to polyurethane foams, who complained of wheezing and breathlessness at work were tested. Subjects were given 20 to 2000 ug methacholine. Forced expiratory volume in 1 sec was measured. Subjects were challenged with 0.01 ppm **toluene** diisocyanate for 15 min in an atmosphere chamber. Forced expiratory volume in 1 sec was measured. Positive tests were considered as a 15% fall in forced expiratory volume in 1 sec. High sensitivity to methacholine was seen in ten subjects with a 15% fall in forced expiratory volume in 1 sec at <1000 ug; normal subjects responded at 2000 ug. All subjects reacted to **toluene** diisocyanate.
[Cardura F, Moscata G; Brit J Indus Med 41: 552-3 (1984)]**PEER REVIEWED**

Human Toxicity Excerpts :

Sensitized subjects may develop symptoms of asthma after exposure to isocyanates in their place of work. After challenge with isocyanates in the laboratory, sensitized subjects develop immediate, late and dual asthmatic reactions. **Toluene** diisocyanate might cause late asthmatic reactions and increase bronchial responsiveness by causing an acute inflammatory reaction in the airways, and that airway inflammation may be responsible for persistence of occupational asthma induced by isocyanates. To test these hypotheses, sensitized subjects were examined during asthmatic reactions induced by exposure to **toluene** diisocyanate in the laboratory. It was observed that late and dual, but not early, asthmatic reactions are associated with a transient

increase of bronchial responsiveness which is associated with an acute inflammatory reaction of the airways characterized by an increase of neutrophils followed by eosinophils, by an increase of leukotriene B4 and albumin in bronchoalveolar lavage fluid, and that all these effects are inhibited by steroids. Longitudinal studies suggest that the majority of subjects with occupational asthma continue to have persistent asthma months and yrs after the cessation of exposure, and the results of our studies combined with the results of studies performed by others suggest that the persistence of asthma may be related to the persistence of airway inflammation. [Fabbri LM et al; Eur Respir J (Suppl 13): 136-38 (1991)]**PEER REVIEWED**

Human Toxicity Excerpts :

Twelve subjects were studied with inhalation challenge testing to **toluene** diisocyanate because of suspected asthma based on a consistent clinical and occupational history. In seven cases, asthma was documented by a positive inhalation challenge to low levels of **toluene** diisocyanate. Six of the seven reactors had persistent respiratory symptoms and required daily treatment even though they had been removed from isocyanate exposure for intervals as long as 12 years (mean 4.5 years). These six reactors had either dual (four cases) or late bronchospasm (two cases) to less than 20 ppb and all had a positive methacholine or cold air challenge prior to study. The one reactor with a negative methacholine challenge had a positive (immediate) bronchospastic response to a challenge performed one week after removal from isocyanate exposure. Five workers had a negative challenge, two of whom had persistent respiratory symptoms and positive methacholine challenges at the time of inhalation testing. ... Respiratory symptoms may persist following long-term removal from occupational exposure to and are associated with nonspecific bronchial hyperreactivity. The sensitivity may also persist for a long time even in the absence of any additional occupational exposure. Long-term prospective studies of symptomatic isocyanate workers are needed to fully define the extent of this problem. [Moller DR et al; Chest 90 (4): 499 (1986)]**PEER REVIEWED**

Protective Equipment & Clothing :

Recommendations for respirator selection: Condition: At concentrations above the NIOSH REL, or where there is no REL, at any detectable concentration: Respirator Class(es): Any self-contained breathing apparatus that has a full facepiece and is operated in a pressure-demand or other positive pressure-mode. Any supplied-air respirator that has a full facepiece and is operated in a pressure-demand or other positive-pressure mode in combination with an auxiliary self-contained breathing apparatus operated in pressure-demand or other positive-pressure mode. /**Toluene** 2,4-diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

Protective Equipment & Clothing :

Facilities for quickly drenching the body should be provided within the immediate work area for emergency use where there is a possibility of exposure. (Note: It is intended that these facilities provide a sufficient quantity or flow of water to quickly remove the substance from any body areas likely to be exposed. The actual determination of what constitutes an adequate quick drench facility depends on the specific circumstances. In certain instances, a deluge shower should be readily available, whereas in others, the availability of water from a sink or hose could be considered adequate.) /**Toluene** 2,4-diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

Protective Equipment & Clothing :

Eyewash fountains should be provided in areas where there is any possibility that workers could be exposed to the substance; this is irrespective of the recommendation involving the wearing of eye protection. /**Toluene** 2,4-diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government

Printing Office, 1997. 313]**QC REVIEWED**

Protective Equipment & Clothing :

Wear appropriate personal protective clothing to prevent skin contact. /**Toluene** 2,4-diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

Protective Equipment & Clothing :

Wear appropriate eye protection to prevent eye contact. /**Toluene** 2,4-diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

Skin, Eye and Respiratory Irritations :

AS A VAPOR ... /**TOLUENE** DIISOCYANATE/ IS A POWERFUL IRRITANT TO EYES, SKIN, RESPIRATORY TRACT.
[Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984.,p. II-414]**PEER REVIEWED**

Hazardous Reactivities & Incompatibilities :

Strong oxidizers, water, acids, bases and amines (may cause foam and splatter); alcohols. [Note: Reacts slowly with water to form carbon dioxide and polyureas.] /**Toluene** 2,4-diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

U. S. Exports :

(1984) 6.27x10+10 g /**TOLUENE** DIISOCYANATES/
[BUREAU OF THE CENSUS. U.S. EXPORTS (1984) p.2-73]**PEER REVIEWED**

Consumption Patterns :

CHEMICAL PROFILE: **Toluene** diisocyanate. Demand: 1986: 650 million lb; 1987: 695 million lb; 1991 /projected/: 720 million lb (Includes exports, imports are negligible).
[Kavaler AR; Chemical Marketing Reporter 232 (25): 50 (1987)]**PEER REVIEWED**

Odor Threshold :

TOLUENE DIISOCYANATE HAS MARKED CHARACTERISTIC ODOR WHICH ALLOWS IT TO BE DETECTED READILY. YET @ MAX RECOMMENDED CONCN (0.02 PPM) THE POISON CANNOT BE DETECTED BY ITS SMELL.
[Lefaux, R. Practical Toxicology of Plastics. Cleveland: CRC Press Inc., 1968. 102]**PEER REVIEWED**

Consumption Patterns :

CHEMICAL PROFILE: **Toluene** Diisocyanate. Flexible urethane foams, 65%; (furniture, 28%; transportation, 16%; carpet underlay, 9%; bedding, 6%; other foam uses, 6%;) exports, 22%; rigid foams, 5%; polyurethane coatings, 4%; elastomers, 2%; miscellaneous non-foam uses, 2%.
[Kavaler AR; Chemical Marketing Reporter 232 (25): 50 (1987)]**PEER REVIEWED**

Manufacturers :

Olin Corporation, 120 Long Ridge Road, Stamford, CT 06904, (203) 356-2000 /**Toluene** 2,4- and 2,6-diisocyanate (80/20) mixture/

[United States International Trade Commission. Synthetic Organic Chemicals-United States Production and Sales, 1991. USITC Publication 2607, February 1993.Washington, DC: United States Trade Commission, 1993.,p. 3-8]**PEER REVIEWED**

Preventive Measures :

The worker should immediately wash the skin when it becomes contaminated. /**Toluene** 2,4-diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

Preventive Measures :

The worker should wash daily at the end of each work shift. /**Toluene** 2,4-diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

Preventive Measures :

Work clothing that becomes wet or significantly contaminated should be removed and replaced. /**Toluene** 2,4-diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

Preventive Measures :

Workers whose clothing may have become contaminated should change into uncontaminated clothing before leaving the work premises. /**Toluene** 2,4-diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

Manufacturers :

Dow Chemical Co, 2020 Willard H. Dow Center, Midland, MI 48674, (517) 636-6125 /**Toluene** 2,4- and 2,6-diisocyanate (80/20) mixture/
[United States International Trade Commission. Synthetic Organic Chemicals-United States Production and Sales, 1991. USITC Publication 2607, February 1993.Washington, DC: United States Trade Commission, 1993.,p. 3-8]**PEER REVIEWED**

Manufacturers :

ICI Americas, Inc., Polyurethane Group 286 Manuta Grove Road, W. Deptford, NJ 08066-1732. (609) 423-8300; Speciality Product Division Concord Pike & Murphy Rd, Willmington, DE 19897, (302) 886-3000 /**Toluene** 2,4- and 2,6-diisocyanate (80/20) mixture/
[United States International Trade Commission. Synthetic Organic Chemicals-United States Production and Sales, 1991. USITC Publication 2607, February 1993.Washington, DC: United States Trade Commission, 1993.,p. 3-8]**PEER REVIEWED**

Manufacturers :

BASF Corporation, Chemicals Division, 1255 Broad St., Cliftn, NJ 07015, (201) 316-2937 /**Toluene** 2,4- and 2,6-diiscyanate (80/20) mixture/
[United States International Trade Commission. Synthetic Organic Chemicals-United States Production and Sales, 1991. USITC Publication 2607, February 1993.Washington, DC: United States Trade Commission, 1993.,p. 3-8]**PEER REVIEWED**

Methods of Manufacturing :

From **toluene** diamine by reaction with carbonyl chloride (phosgene)
[Zenz, C. Occupational Medicine-Principles and Practical Applications. 2nd ed. St. Louis, MO: Mosby-Yearbook, Inc, 1988. 1016]**PEER REVIEWED**

Major Uses :

POLYURETHANE COATINGS MADE FROM **TOLUENE** DIISOCYANATE MIXT ... IN GENERAL ... ARE USED IN FLOOR FINISHES, WOOD FINISHES & SEALERS, TRADE SALES PAINTS, CONCRETE SEALERS, & IN COATINGS FOR AIRCRAFT, TANK TRUCKS, TRUCK TRAILERS & TRUCK FLEETS. /MIXT OF 2,4- & 2,6-ISOMERS/
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V19 307 (1979)]**PEER REVIEWED**

Protective Equipment & Clothing :

Recommendations for respirator selection: Escape from suddenly occurring respiratory hazards: Respirator Class(es): Any air-purifying, full-facepiece respirator (gas mask) with a chin-style, front- or back-mounted organic vapor canister. Any appropriate escape-type, self-contained breathing apparatus. /**Toluene** 2,4-diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

Manufacturers :

Rubicon, Inc, PO Box 517, Geismar, LA 70734, (504) 673-6141 /**Toluene** 2,4- and 2,6-diisocyanate (80/20) mixture/
[United States International Trade Commission. Synthetic Organic Chemicals-United States Production and Sales, 1991. USITC Publication 2607, February 1993.Washington, DC: United States Trade Commission, 1993.,p. 3-8]**PEER REVIEWED**

Methods of Manufacturing :

NITRATION OF **TOLUENE**, FOLLOWED BY REDUCTION TO DIAMINE, REACTION WITH PHOSGENE, PURIFICATION, AND RECOVERY OF COPRODUCT HYDROGEN CHLORIDE.
[CHEM & ENG NEWS 63 (37): 16 (1985)]**PEER REVIEWED**

Fire Potential :

DUE TO ITS HIGH FLASH POINT, **TOLUENE** DIISOCYANATE OFFERS NO SERIOUS RISK OF FIRE ... .
[Lefaux, R. Practical Toxicology of Plastics. Cleveland: CRC Press Inc., 1968. 103]**PEER REVIEWED**

Human Toxicity Excerpts :

Symptoms and lung function of workers exposed to isocyanates in polyurethane foam factories were studied. A group of 67 workers was examined for **toluene**-diisocyanate ... exposure. Measurements were made by samples obtained from subject carried pumps. Interviews were also conducted for information of symptoms involving the nose, eyes, upper airways, and lung. Another group of 56 nonexposed workers was determined by spirometry and nitrogen wash out prior to the work shift. The exposed workers were examined again immediately after work. The variables studied were forced expired vital capacity and forced expired volume in 1 second. ... The highest exposure group was foaming machine workers, with a day mean exposure of 0.023 mg/cu m. Nonsmokers showed an increased frequency of symptoms involving the nose, throat, and dyspnea. Smokers had no significant increase. Smokers of the exposed group reported coughing. Only smokers reported symptoms classified as chronic bronchitis, with frequency independent of exposure. Decreased forced expired vital capacity and forced expired volume were observed in the exposed group. This group also showed increased expired vital capacity.

Lung function impairment was restricted to smokers. Spirometric and nitrogen washout variables did not change significantly during the work shift. Decreasing spirometric values with increased exposure was seen in smokers. Conclusions indicate that mean exposure of 0.01 mg/cu m/day to isocyanates may give an increased frequency of symptoms in nonsmokers.
[Alexanderson R et al; Internat Archives of Occup Environ Health 55 (2): 149-57 (1985)]**PEER REVIEWED**

Special Reports :

Kay S; Food and Chemical Toxicology 23 (3): 411-13. (1985) **Toluene** diisocyanate and Lung Function.

Analytic Laboratory Methods :

DETERMINATION OF **TOLUENE** DIISOCYANATE (TDI) IN AIR BY LC. MAX SENSITIVITY IS OBSERVED AT AN EXCITATION WAVELENGTH OF 226 NM & USING A 300-NM CUT-OFF EMISSION FILTER. A DETECTION LIMIT OF 0.4 PPB FOR TDI CAN BE ACHIEVED WITH A 1 L AIR SAMPLE.
[KORMOS LH ET AL; ANAL CHEM 53 (7): 1122 (1981)]**PEER REVIEWED**

Disposal Methods :

Toluene diisocyanate is a waste chemical stream constituent which may be subjected to ultimate disposal by controlled incineration. Controlled incineration: Oxides of nitrogen are removed from the effluent gas by scrubbers and/or thermal devices.
[USEPA; Engineering Handbook for Hazardous Waste Incineration p.2-10 (1981) EPA 68-03-3025]**PEER REVIEWED**

Analytic Laboratory Methods :

GASES IN THE ATMOSPHERE ARE MONITORED WITH CHEMICALLY-COATED QUARTZ PIEZOELECTRIC CRYSTALS; THE METHOD IS DEMONSTRATED IN THE USE OF POLYETHYLENE GLYCOL FOR **TOLUENE** DIISOCYANATE DETERMINATION. A MICROPROCESSOR IS USED TO CONTROL THE GAS SAMPLE FLOW THROUGH THE DETECTOR HEAD AS WELL AS THE DATA ACQUISITION. THE THEORETICAL DETECTION LIMIT IS APPROX 0.006 PPM.
[ALDER JF, ISAAC CA; ANAL CHIM ACTA 129 (1): 175 (1981)]**PEER REVIEWED**

Analytic Laboratory Methods :

DETERMINATION OF **TOLUENE** DIISOCYANATE WORKING ATMOSPHERES BY HPLC USING UV OR FLUORESCENCE DETECTION. THE DETECTION LIMIT IS APPROX 1X10-4 MG/CU M.
[SANGOE C, ZIMERSON E; J LIQ CHROMATOGR 3 (7): 971 (1980)]**PEER REVIEWED**

Non-Human Toxicity Excerpts :

Rats receiving up to 240 mg/kg **toluene** diisocyanate by gavage daily on 5 days/wk for 13 wk were found to suffer from mild to moderate bronchopneumonia.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 306 (1986)]**PEER REVIEWED**

Sampling Procedures :

EPA Method 8020. For the analysis of solid waste, a representative sample (solid or liquid) is collected in a standard 40 ml glass screw cap VOA vial equipped with a Teflon faced silicone septum. Sample agitation, as well as contamination of the sample with air, must be avoided. Two vials are filled per sample location, then placed in separate plastic bags for shipment and storage. /**Toluene**/
[USEPA; Test Methods for Evaluating Solid Waste SW-846

(1986)]**PEER REVIEWED**

Non-Human Toxicity Excerpts :

Groups of 120 male and 120 female CD-1 mice, three to four weeks old, were exposed to 0, 0.05, or 0.15 ppm (0, 0.36 or 1.07 mg/cu m) production grade **toluene** diisocyanate (approx 80% 2,4 isomer & 20% 2,6 isomer) in an inhalation chamber for 6 hr/day on 5 days/wk for 104 wk. There was a significant reduction in body weight in the high-dose group /sex not stated/ and a significant increase in mortality in both high and low-dose females by the termination of the study. No such effect was seen in males. Neither the types of tumor observed nor their incidences were dose-related, and both corresponded to those seen in historical controls for this strain of mice. However, dose-related pathological changes were observed in the nasal cavity (chronic or necrotic rhinitis), together with changes in the lower respiratory tract (interstitial pneumonia, catarrhal bronchitis) in both groups.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 303 (1986)]**PEER REVIEWED**

Non-Human Toxicity Excerpts :

Groups of 126 male and 126 female Sprague Dawley CD rats, six to nine weeks old, were exposed to 0, 0.05 or 0.15 ppm (0, 0.36 or 1.07 mg/cu m) production-grade **toluene** diisocyanate (approx 80% 2,4 isomer and 20% 2,6 isomer) in an inhalation chamber for 6 hr/day on 5 days/wk for 108 wk or 110 wk. A significant reduction in weight gain was observed during the first 12 wk of the study among the high-dose animals of each sex, but body wt gain was similar in all groups thereafter. No significant difference in mortality between treated and control groups of either sex was reported. Tumor incidences and types were reported to be similar in control and treated groups.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 304 (1986)]**PEER REVIEWED**

NIOSH Recommendations :

NIOSH usually recommends that occupational exposures to carcinogens be limited to the lowest feasible concentration. /2,4-**Toluene** diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

Probable Routes of Human Exposure :

THE RESPIRATORY HEALTH OF 277 WORKERS IN A NEW **TOLUENE** DIISOCYANATE (TDI) MANUFACTURING PLANT WAS STUDIED PROSPECTIVELY DURING 5 YR OF EXPOSURE. PERSONAL TDI MONITORS WERE USED TO CONTINUOUSLY MEASURE PEAK & 8-HR TIME-WEIGHTED AVG (TWA) CONCN IN MORE THAN 2000 SAMPLES. REGRESSION OF ANNUAL CHANGE ON SMOKING (PACK-YEARS), ATOPIC STATUS & CUMULATIVE TDI EXPOSURE, DICHOTOMIZED AT 68.2 PPB MONTHS INTO LOW & HIGH EXPOSURE GROUPS, SHOWED SIGNIFICANT EFFECTS OF SMOKING ON SPIROMETRIC TESTS & LUNG VOLUMES. AFTER ADJUSTING FOR PACK-YEARS OF SMOKING, THE 74 MEN IN THE HIGH CUMULATIVE TDI EXPOSURE CATEGORY HAD SIGNIFICANTLY LARGER DECLINE IN FEV1 (1-S FORCED EXPIRATORY VOLUME), % FEV (% FORCED EXPIRATORY VOLUME) & FEF25-75% (FORCED EXPIRATORY FRACTION FROM 25 TO 75% VITAL CAPACITY) THAN DID THE 149 MEN IN THE LOW CATEGORY. ANNUAL CHANGE IN FEV1 WAS THEN EXAMINED IN 6 SMOKING-EXPOSURE CATEGORIES: IN NEVER-SMOKERS, AVG ANNUAL DECLINE WAS 38 ML/YR GREATER IN THOSE WITH HIGHER CUMULATIVE TDI EXPOSURE.
[DIEM JE ET AL; AM REV RESPIR DIS 126 (3): 420 (1982)]**PEER REVIEWED**

Probable Routes of Human Exposure :

Exposure to **toluene** diisocyanate is primarily occupational via inhalation or dermal contact with the aerosol or vapor. Workers may also be exposed through skin contact with freshly cured foam or as a result of spills or splashes. (SRC)
PEER REVIEWED

Natural Pollution Sources :

2,4- and 2,6-**toluene** diisocyanate, the components of commercial TDI are not known to occur as a natural product(1).
[(1) IARC; Monograph on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. 19: 303-11 (1979)]**PEER REVIEWED**

Human Toxicity Excerpts :

A shortened protocol was developed for the epidemiological measurement of bronchial responsiveness to methacholine without compromising sensitivity, power, precision or safety, and without distorting the numerical value of the PD20.FEV1 (the cumulative dose from a doubling incremental sequence which provokes a 20% decrement in forced expiratory volume in 1 second). It was used in a survey of 254 polyurethane workers (83% of the eligible workforce) exposed occupationally to **toluene** diisocyanate. The mean duration of each test proved to be 38 min, it was well tolerated and 64 workers (25%) proved to be reactors. PD20.FEV1 appeared to be distributed unimodally. It was significantly correlated with questionnaire records of shortness of breath, chest tightness, and wheeze; and with pre-shift forced expiratory volume in 1 second and FEF25-75. Even the reactors requiring the highest dose of 640 cumulative inhalation units (1 unit = one 8.9 ul inhalation of methacholine 1 mg/ml) to generate a PD20 measurement reported significantly more wheeze than the non-reactors. This indicates that the test had clinical meaning throughout its dose range of 0.3-640 units. No correlation was found between PD20 and individual changes in ventilatory function across the working shift, but mean shift changes were negligible and not statistically significant. PD20 was also found to be unrelated to age, sex, race, smoking, cough and atopy.
[Hendrick DJ; Bull Eur Physiopathol Respir 23 (6): 555-9 (1987)]**PEER REVIEWED**

Analytic Laboratory Methods :

Isocyanate determination air paper tape Hydrazine determination air paper tape;Air analysis Hydrazine deriv. and **toluene** diisocyanate determination. in, miniature paper tape apparatus for
[Hughes WT Jr; Anal Instrum (Research Triangle Park, N. C.) 22: 87-98 (1986)]**PEER REVIEWED**

Non-Human Toxicity Excerpts :

Toluene diisocyanate was mutagenic in Salmonella typhimurium strains TA98 and TA100 in the presence (but not the absence) of Aroclor 1254-induced male Sprague Dawley rat or male Syrian hamster liver S9; it was not mutagenic in strains TA 1535 or 1537.
[DHHS/NTP; Toxicology and Carcinogenesis Studies of Commercial Grade 2,4 (80%) and 2,6 (20%) - Toluene Diisocyanate (Gavage Studies) p. 7 (1986) Technical Rpt Series No. 251 NIH Pub No. 86-2507]**PEER REVIEWED**

Medical Surveillance :

A SCREENING PROGRAM WAS UNDERTAKEN AT A RESEARCH & DEVELOPMENT FACILITY OF A LARGE **TOLUENE**-DIISOCYANATE (TDI) MANUFACTURING CORPORATION. THE PURPOSE WAS TO DETERMINE THE OCCURRENCE OF ANTIBODIES TO TDI IN SELECTED WORKER POPULATIONS. NO TOLYL-REACTIVE IMMUNOGLOBULIN-E ANTIBODIES WERE DETECTED IN SERA WHEN WORKERS WERE EXPOSED ONLY TO AMBIENT TDI CONCN. WORKERS HAD ACUTE EXPOSURES TO TDI AS A RESULT OF SPILLS OR SPLASHES. ANTIBODY RESPONSES DEVELOPED IN 3 OF 4 INDIVIDUALS WHOSE ACUTE EXPOSURES WERE ACCOMPANIED BY IMMEDIATE RESPIRATORY SYMPTOMATOLOGY & A DECREASED FORCED EXPIRATORY VOLUME. AN ANTIBODY RESPONSE

DEVELOPED IN 1 OF 9 WORKERS & IMMEDIATE RESPIRATORY SYMPTOMS, BUT NO SPIROMETRIC CHANGES UPON ACUTE TDI EXPOSURE. ROUTINE SEROLOGIC SCREENING OF WORKERS FOR TOLYL-REACTIVE ANTIBODIES MAY BE OF VALUE IN CONFIRMING SUSPECTED ISOCYANATE EXPOSURE & IN PROVIDING AN EARLY WARNING OF DEVELOPING TDI HYPERSENSITIVITY.
[KAROL MH; J OCCUP MED 23 (11): 741 (1981)]**PEER REVIEWED**

Sampling Procedures :

NIOSH Method: 5505. Analyte: 1-(2-methoxyphenyl)piperazine; HCO group. Matrix: Air. Sampler: Impinger (solution of 1-(2-methoxyphenyl)-piperazine in **toluene**). Flow Rate: 1 l/min. Sample Size: 600 liters. Shipment: In vials; flammable liquid. Sample Stability: Equal to or greater than 2 weeks. /Isocyanate group/
[U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. 5505-1]**PEER REVIEWED**

Medical Surveillance :

/Protect/ from exposure those individuals with diseases of blood and liver. Physical exam of exposed personnel annually, incl blood count and liver functions. /**Toluene**-2,4-diisocyanate/
[ITII. Toxic and Hazardous Industrial Chemicals Safety Manual. Tokyo, Japan: The International Technical Information Institute, 1988. 528]**PEER REVIEWED**

Analytic Laboratory Methods :

TOLUENE DIISOCYANATE ... DETERMINED IN ... ATMOSPHERE BY TLC.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V19 309 (1979)]**PEER REVIEWED**

RCRA Requirements :

U223; As stipulated in 40 CFR 261.33, when **toluene** diisocyanate, as a commercial chemical product or manufacturing chemical intermediate or an off-specification commercial chemical product or a manufacturing chemical intermediate, becomes a waste, it must be managed according to Federal and/or State hazardous waste regulations. Also defined as a hazardous waste is any residue, contaminated soil, water, or other debris resulting from the cleanup of a spill, into water or on dry land, of this waste. Generators of small quantities of this waste may qualify for partial exclusion from hazardous waste regulations (40 CFR 261.5).
[40 CFR 261.33 (7/1/91)]**PEER REVIEWED**

Human Toxicity Excerpts :

TOLUENE DIISOCYANATE (TDI) SENSITIVITY ACCOMPANIED BY NONSPECIFIC BRONCHIAL HYPERRESPONSIVENESS OCCURS IN 5% OF OCCUPATIONALLY EXPOSED WORKERS. THE CASE OF A 32 YR OLD WORKER FOLLOWED LONGITUDINALLY AFTER REMOVAL FROM ISOCYANATE EXPOSURE IS REPORTED. TDI REACTIVITY WAS LOST 11 MONTHS AFTER REMOVAL FROM EXPOSURE & NONSPECIFIC BRONCHIAL HYPERRESPONSIVENESS RESOLVED AFTER 17 MONTHS. IMMUNOPHARMACOLOGIC RESULTS SHOW THAT THE WORKER'S INITIAL DECREASED ABILITY OF LYMPHOCYTES TO PRODUCE CYCLIC-AMP RETURNED TO NEAR NORMAL AFTER 2 YR. IMMUNOGLOBULIN-E ANTIBODIES TO A HUMAN SERUM ALBUMIN TOLYL MONOISOCYANATE CONJUGATE WERE STILL PRESENT THIS TIME.
[BUTCHER BT ET AL; J ALLERGY CLIN IMMUNOL 70 (4): 231 (1982)]**PEER REVIEWED**

Atmospheric Standards :

This action promulgates standards of performance for equipment leaks of Volatile Organic Compounds (VOC) in the Synthetic Organic Chemical Manufacturing Industry (SOCMI). The intended effect of these standards is to require all newly constructed, modified, and reconstructed SOCMI process units to use the best demonstrated system of continuous emission reduction for equipment leaks of VOC, considering costs, non air quality health and environmental impact and energy requirements. **Toluene** diisocyanate is produced, as an intermediate or a final product, by process units covered under this subpart.
[40 CFR 60.489 (7/1/91)]**PEER REVIEWED**

Probable Routes of Human Exposure :

Concentration medians for 2,4-**toluene** diisocyanate in 2 plants producing flexible polyurethane foam were 0.70 and 0.33 ppb for the mixing and finishing ends, respectively(1). The respective median values for 2,6-TDI were 0.91 and 1.1 ppb. Maximum concentrations of 2,6-TDI exceeded 64 ppb at the finishing end(1).
[(1) Rando RJ et al; Am Ind Hyg Assoc J 45: 199-203 (1984)]**PEER REVIEWED**

Non-Human Toxicity Excerpts :

TOLUENE DIISOCYANATE WAS MUTAGENIC IN SALMONELLA TYPHIMURIUM STRAINS TA1538 & TA98 AFTER METABOLIC ACTIVATION.
[ANDERSEN M ET AL; SCAND J WORK ENVIRON HEALTH 6 (3): 221 (1980)]**PEER REVIEWED**

Artificial Pollution Sources :

Levels of 100-17,700 ug/cu m **toluene** diisocyanate were reported in samples from the stack exhaust of a polyurethane foam production plant.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 299 (1986)]**PEER REVIEWED**

Mechanism of Action :

Serum immunoglobulin-G and immunoglobulin-E to isocyanate haptenized human serum albumin (HSA) were estimated by ELISA in 55 isocyanate workers who underwent isocyanate inhalation challenge studies in Montreal, Canada. The challenges were negative in 29 workers and positive in 26 workers. Isocyanate antibodies were estimated by ELISA index. The mean immunoglobulin-G indices were found to be significantly higher in the challenge-positive workers, and there was a similar trend for the immunoglobulin-E indices. Antibody specificities for **toluene** diisocyanate-human serum albumin, diphenylmethane diisocyanate-human serum albumin, and hexamethylene diisocyanate-human serum albumin were determined by inhibition studies with a variety of isocyanate haptenized carriers. The other isocyanate substituted carriers were either noninhibitory or caused only partial inhibition as contrasted with the complete inhibition achieved by human serum albumin conjugated to the isocyanate to which the worker was exposed. We interpret these specificity studies as indicating that the inhalation of isocyanates results in production of antibody that recognizes new antigenic determinants that develop from the coupling of isocyanates to homologous proteins.
[Grammer LC et al; J Allergy Clin Immunol 86 (1): 94-8 (1990)]**PEER REVIEWED**

Human Toxicity Excerpts :

Subjects exposed to 0.0010 to 0.0015 ppm of **toluene** diisocyanate demonstrated a normal age and smoking-related rate of decline in forced expiratory volume in 1 second and no evidence that it was related to isocyanate exposures.
[Musk AW et al; J Occup Med 27 (12): 917-20 (1985)]**PEER REVIEWED**

Probable Routes of Human Exposure :

VAPORS OF THESE COMPD INVARIABLY BECOME AIRBORNE IN POLYMERIZATION REACTIONS, ESP SINCE HEAT & GAS ARE EVOLVED. /**TOLUENE** DIISOCYANATES/
[Hamilton, A., and H. L. Hardy. Industrial Toxicology. 3rd ed. Acton, Mass.: Publishing Sciences Group, Inc., 1974. 335]**PEER REVIEWED**

Human Toxicity Excerpts :

Two workers who developed asthmatic symptoms were studied with inhalation provocation tests using ... **toluene** diisocyanate. Subjects did not show asthmatic reations to TDI challenge.
[Mapp CE et al; Ann Allergy 54 (5): 424-9 (1985)]**PEER REVIEWED**

Human Toxicity Excerpts :

Respiratory variables were measured in workers exposed to **toluene** diisocyanate in Canada. Exposure and effect relationships were studied. Results from 95 isocyanate workers were compared with unexposed workers. Exposed workers were grouped according to production areas based on isocyanate concentrations measured. Individual monitors were worn to identify exposure for some workers. Symptoms and history of respiratory illness were compared through questionnaires. Pulmonary function tests included forced vital capacity, forced expiratory volume in 1 second, and forced expiratory flow at 50% and 75% of vital capacity. Pulmonary function was measured at the beginning and end of work shifts on Monday, Wednesday, and Friday of a work week. Regression analysis of exposure concentration and other variables was attempted. When comparisons were adjusted for smoking habits, exposed workers had a significantly lower family history of respiratory complaints. Isocyanate workers had slightly lower base line lung function than comparisons, but had significantly higher declines in pulmonary function over the work week. A 5% or greater decline over a day occurred in 44 percent of exposed but only 22% of comparison workers. Foam line and finishing area workers had greatest declines in forced vital capacity and forced expiratory volume in 1 second. It was concluded that although regression analysis does not show an exposure/effect relationship, an all or none effect may be operating with acute and chronic compartments. However, sample size may have been insufficient.
[Holness DL et al; J Occup Med 26 (6): 449-55 (1984)]**PEER REVIEWED**

Human Toxicity Excerpts :

... The toxicity of inhaled vapors of diisocyanates is summarized. Humans are exposed to high concentrations of diisocyanates in polyurethane industries. Toxic symptoms are acute inflammation with lachrymation, rhinitis, soreness and burning in the throat and upper part of the chest, and coughing. Fire fighters are particularly prone to these clinical symptoms. The toxic limit value for **toluene** diisocyanate is 0.005 ppm. Exposure to diisocyanates can cause asthma.
[Davies RJ; Clinics in Immunology and Allergy 4 (1): 103-23 (1984)]**PEER REVIEWED**

Environmental Water Concentrations :

Toluene diisocyanate has been reported in the waste-water of a furniture manufacturing area in a concn range of 0.1-4.1 mg/l.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 299 (1986)]**PEER REVIEWED**

Human Toxicity Excerpts :

Toluene diisocyanate may produce a true hemorrhagic syndrome affecting the bone marrow and producing primarily thrombocyte series suppression.
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland:

International Labour Office, 1983. 303]**PEER REVIEWED**

Human Toxicity Excerpts :

Technical grade **toluene** diisocyanate induced chromosome aberrations after a 24 hr treatment in the absence of metabolic activation in human whole blood lymphocyte cultures.
[Maki-Paakkanen J, Norppa H; Toxicol Lett 36 (1): 37-43 (1987)]**PEER REVIEWED**

Environmental Fate :

TERRESTRIAL FATE: Ten days after a spill of 13 tons of **toluene** diisocyanate (TDI) onto swampy, wet forest soil, TDI and toluenediamines were found in the soil(1,2). The TDI solidified and the area was covered with sand. The soil concn of TDI and toluenediamine combined declined from the parts per thousand to parts per million range between 10 days and 12 wk after the spill(2). No TDI was detected in a connecting brook 10 days after the spill(2). After 6 years only TDI-derived polyureas were found at the site(1). In a simulated spill, 5 kg of TDI in a container was covered with 50 kg of sand and 5 kg of water at ambient temperatures and samples taken from the top and bottom of the sand pile. After 24 hr, 5.5% of the TDI remained unreacted and after 8 days 3.5% remained(2). The reaction product was largely polyureas(2).
[(1) IARC Monograph on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. 39: 287-323 (1985) (2) Brochhagen FK, Grieveson BM; Cellular Ploymers 3: 11-7 (1984)]**PEER REVIEWED**

Human Toxicity Excerpts :

Case reports of keratophathy in polyurethane production workers were examined. The experimental production of similar conditions was studied in cats and a monkey. A male polyurethane worker complained of blurred vision which improved over weekends away from work. The only significant finding on examination of the eyes was subepithelial corneal vesicles of 30 to 50 micrometers in diameter. A second patient, a female worker from the same facility, also complained of attacks of blurred vision. Slit lamp examination showed deep or subepithelial vacuolization only in the palpebral aperture. ... Corneas were normal between 3 day and 2 weeks. Exposure to **toluene** diisocyanate did not result in the clinical appearance of the eye resembling that of the workers.
[Potts AM et al; Am J Indust Med 9 (2): 203-13 (1986)]**PEER REVIEWED**

Analytic Laboratory Methods :

Matrix: Air. Sample preparation: Draw air through impinger containing aq acid; neutralize; extract (chloroform or **toluene**); react with trifluoroacetic anhydride or heptafluorobutyric anhydride. Procedure: GC/ECD. Limit of detection: 1-5 ug/cu m. /From table/
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 300 (1986)]**PEER REVIEWED**

Special Reports :

Toluene diisocyanate; Safety Practitioner 3 (5): 32-3 (1985).

Special Reports :

DHHS/NTP; Toxicology & Carcinogenesis Studies of Commercial Grade 2,4 (80%)- and 2,6 (20%)-**Toluene** Diisocyanate in F344/N Rats and B6C3F1 Mice(Gavage Studies) Technical Report Series No. 251 (1986) NIH Publication No. 86-2507

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HSDB Search Results

for Toluene 108-88-3

Query:

Information added from CHEMID:
Chemid Name: **toluene [108-88-3]**
(toluol, methylbenzene, toluen, tolueen, phenylmethane, methylbenzol, methacide)
toluene (toluol, methylbenzene, tolueen, phenylmethane, methylbenzol, methacide)

Registry Numbers:
108-88-3 108-88-3
~
1 record contains the exact substance name or CAS registry number.
671 records contain all of the query terms anywhere in the record.

Items **1** through **20** of **672** **Pages:** 1 3 5 7 9 11 13 15 17 19 21 23 25 27 29 31 33 35

*Substance Names are sorted in **relevancy ranked** order.*

	Substance Name

The following is the primary record for the chemical. All of the query terms were found.

1 **TOLUENE**
108-88-3

The following 671 records contain one or more of the requested chemical name(s) and all of the query terms anywhere in the record.

2 **TOLUENE DIISOCYANATE**
26471-62-5

3 **2,4-TOLUENE DIISOCYANATE**
584-84-9

4 **2,6-TOLUENE DIISOCYANATE**
91-08-7

5 **VINYL TOLUENE**
25013-15-4

6 **TOLUENE-2,4-DIAMINE**
95-80-7

7 **o-CRESOL**
95-48-7

8 **BENZENE**
71-43-2

9 **1-METHOXY-4-METHYLBENZENE**
104-93-8

10 **XYLENE**
1330-20-7

11 **HEXAMETHYLENE DIISOCYANATE**
822-06-0

12 **4-VINYLTOLUENE**
622-97-9

13 **2,6-DIAMINOTOLUENE**
823-40-5

14 **3,5-DIAMINOTOLUENE**
108-71-4

15 **BENZOIC ACID**
65-85-0

16 **4-XYLENE**
106-42-3

17 **STYRENE**
100-42-5

18 **3-XYLENE**
108-38-3

19 **4-T-BUTYLTOLUENE**
98-51-1

20 **3-BROMOTOLUENE**
591-17-3

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TOLUENE

CASRN: 108-88-3

For other data, click on the Table of Contents

Synonyms:

TOLUEN (CZECH)

PEER REVIEWED

TOLUENE

CASRN: 108-88-3

For other data, click on the Table of Contents

Synonyms:

TOLUEEN (DUTCH)

PEER REVIEWED

TOLUENE

CASRN: 108-88-3

For other data, click on the Table of Contents

Human Health Effects:

Evidence for Carcinogenicity:

Evaluation: There is inadequate evidence for the carcinogenicity of **toluene** in humans. There is evidence suggesting lack of carcinogenicity of **toluene** in experimental animals. Overall evaluation: **Toluene** is not classifiable as to its carcinogenicity to humans (Group 3).
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V71 855 (1999)]**PEER REVIEWED**

CLASSIFICATION: D; not classifiable as to human carcinogenicity. BASIS FOR CLASSIFICATION: No human data and inadequate animal data. **Toluene** did not produce positive results in the majority of genotoxic assays. HUMAN CARCINOGENICITY DATA: None.
[U.S. Environmental Protection Agency's Integrated Risk Information System (IRIS) on Toluene (108-88-3) Available from: http://www.epa.gov/ngispgm3/iris on the Substance File List as of March 15, 2000]**PEER REVIEWED**

A4. A4= Not classifiable as a human carcinogen.
[American Conference of Governmental Industrial Hygienists. TLVs and BEIs. Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. Cincinnati, OH. 2000. 67]**QC REVIEWED**

Human Toxicity Excerpts:

Among 61 painters inhaling 100-1100 ppm **toluene** for 2 wk to 5 yr, depressed erythrocyte counts with elevated hemoglobin, mean corpuscular volumes, and elevated mean corpuscular hemoglobin were found in 5% to 30% compared with groups of 73-395 workers not known to be exposed to **toluene**; differential leukocyte counts were not significantly different between the **toluene**-exposed and the reference workers.
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Volumes I,II, III. Cincinnati, OH: ACGIH, 1991. 1573]**PEER REVIEWED**

... **TOLUENE** CAUSES DEFATTING OF SKIN WITH SUBSEQUENT DANGER OF DRYNESS, FISSURING AND SECONDARY INFECTION.
[International Labour Office. Encyclopedia of Occupational Health and Safety. Volumes I and II. New York: McGraw-Hill Book Co., 1971. 1414]**PEER REVIEWED**

... SUDDEN DEATH AMONG "SNIFFERS" MAY BE ATTRIBUTED TO LETHAL CARDIAC ARRHYTHMIAS FOLLOWING SENSITIZATION OF THE MYOCARDIUM.
[Hamilton, A., and H. L. Hardy. Industrial Toxicology. 3rd ed. Acton, Mass.: Publishing Sciences Group, Inc., 1974. 276]**PEER REVIEWED**

... PERMANENT ENCEPHALOPATHY ... /IN/ MAN WHO INHALED **TOLUENE** REGULARLY FOR OVER 14 YR /WAS DESCRIBED/.
[American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices. 5th ed. Cincinnati, OH:American Conference of Governmental Industrial Hygienists, 1986. 578]**PEER REVIEWED**

VAPORS OF **TOLUENE** CAUSE NOTICEABLE SENSATION OF IRRITATION TO HUMAN EYES AT 300-400 PPM IN AIR, BUT EVEN AT 800 PPM IRRITATION IS SLIGHT. ... IN HUMAN VOLUNTEERS EXPOSED TO CONCN AS HIGH AS 800 PPM ... DILATION OF PUPILS & IMPAIRMENT OF REACTION IN ASSOCIATION WITH FATIGUE AT END OF 8 HR, ALSO SLIGHT PALLOR OF FUNDI.
[Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986. 927]**PEER REVIEWED**

Metabolic acidosis with a high "anion gap" in 2 patients who had been sniffing **toluene**.
[Reynolds, J.E.F., Prasad, A.B. (eds.) Martindale-The Extra Pharmacopoeia. 28th ed. London: The Pharmaceutical Press, 1982. 1455]**PEER REVIEWED**

A report of 2 children who sniffed glue containing **toluene**. One of the children became comatose after an episode of "sniffing" which lasted for several hours. Adverse effects included reduced appetite, nightmares, vertical nystagmus, and incoordination.
[Reynolds, J.E.F., Prasad, A.B. (eds.) Martindale-The Extra Pharmacopoeia. 28th ed. London: The Pharmaceutical Press, 1982. 1455]**PEER REVIEWED**

WORKERS IN PHARMACEUTICAL PLANT IN FRANCE EXPOSED TO **TOLUENE** DEVELOPED LEUKOPENIA, & NEUTROPENIA. WITHIN 6 MO, THOSE AFFECTED SHOWED INCR IN CLOTTING TIME & DECR IN PROTHROMBIN LEVEL ...
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1329]**PEER REVIEWED**

PERIPHERAL BLOOD LYMPHOCYTES FROM 32 MALE ROTOGRAVURE WORKERS SHOWED NO SIGNIFICANT DIFFERENCE FROM CONTROLS IN FREQUENCY OF CHROMOSOME ABERRATIONS & SISTER CHROMATID EXCHANGES.
[MAKI-PAAKKANEN J ET AL; J TOXICOL ENVIRON HEALTH 6: 775 (1980)]**PEER REVIEWED**

Patients (3) with history of recurrent **toluene** abuse were hospitalized and severe metabolic acidosis, electrolyte abnormalities, hypoalkemia, and muscular weakness were present. Distal renal tubular acidosis was believed to be present in 2/3 patients.

[Fiscman CM, Oster JR; Am Med Assoc 241 (16): 1713-15 (1979) as cited in NRC; Alkyl Benzenes p.284 (1981)]**PEER REVIEWED**

Child of a mother with a 14 year history of solvent abuse showed symptoms of fetal alcohol syndrome.
[Toutant C, Lippman S; Lancet 1 (8130): 1356 (1979)]**PEER REVIEWED**

A 27-year-old male developed cerebral and cerebellar atrophy over a period of five years of extensive glue sniffing. He also developed bilateral optic atrophy with blindness and severe sensorineural hearing loss.
[Ehyai A, Freemon FR; J Neural Neurosurg Psychiatry 46 (4): 349-51 (1983)]**PEER REVIEWED**

Toluene appears to produce reversible effects upon liver, renal, and nervous systems. ... The nervous system appears to be the most sensitive to the effects of **toluene**. ... High level **toluene** exposures produced incoordination, ataxia, unconsciousness and eventually, death. Lower level acute exposures in man produce dizziness, exhilaration and confusion. Activity level has been inadequately studied. Schedule controlled behaviors have been reported to produce inverted U-shaped concentration-effect curves on response rate measures. Alterations at levels as low as 150 ppm have been reported when appetitive contingencies are used. Very few studies of the nervous system have been performed at levels below 1000 ppm and most of the results were inconclusive. ...
[Benignus VA; Neurobehav Toxicol Teratol 3 (4): 407-15 (1981)]**PEER REVIEWED**

Lethal levels 1.0 mg%; 10.0 ug/ml
[Winek, C.L. Drug and Chemical Blood-Level Data 1985. Pittsburgh, PA: Allied Fischer Scientific, 1985.]**PEER REVIEWED**

IN EXPERIMENTS IN VITRO, **TOLUENE** DID NOT CHANGE NUMBER OF SISTER-CHROMATID EXCHANGES OR THE NUMBER OF CHROMOSOMAL ABERRATIONS IN HUMAN LYMPHOCYTES.
[GERNER-SCMIDT P, FRIEDRICH U; MUTATION RESEARCH 58: 313 (1978)]**PEER REVIEWED**

A 28 yr old painter who was believed to be a habitual **toluene** sniffer was admitted to Chiba Emergency Medical Center on several occasions. Symptoms included: Tremors of the upper extremeties, staggering of gait, slurred speech, slight mental deterioration, pendular nystagmus, bradycardia, mild tremor of the leg, action myoclonus, and head and trunchal titubation. There was no dysmetria. The involuntary movements were classified as hyperkinesie volitionnelle. Muscle tone was hypotonic. Muscle weakness and atrophy were not seen. Deep tendon reflexes were all exaggerated, but there was no pathological reflex. He showed wide-based ataxic gait. Sensory and autonomic functions were normal. Blood, urine and cerebrospinal fluid analysis appeared normal. Electroencephalography showed 40-50 uV, 9-10 c/s alpha waves with a few fast waves. Brain CT scan revealed a moderate enlargement of the lateral and third ventricles. Surface electromyography was performed on the proximal musculature of the arm. 3 c/s reciprocal rhythmical grouping discharges were found at the terminal phase of the elbow bending. The tremor was diminished by 20 minutes ischemic compression test of the arm. With respect to therapy, clonazepam was useful for hyperkinesie volitionnelle. He became able to drink a cup of water without spilling it by his own hands, and was discharged from hospital on April 3rd, 1981. It was believed that he was a habitual sniffer to **toluene**. On June 30th, 1983 he was found comatose. On admission to Chiba

Emergency Medical Center, his breath smelt of **toluene**. His blood **toluene** level was 7.53 ppm, and urinary hippuric acid concentration was 9,500 mg/l. He died on July 9th, 1983, because of disseminated intravascular coagulation, multiple organ failure and perforation of the terminal ileum. Autopsy was performed and neuropathological findings were as follows. 1) Diffuse demyelination and gliosis of the cerebral and cerebella white matter. 2) Marked loss of Purkinje cells of the cerebellum. 3) Astrocytic proliferation of the dentate fugal system and inferior olivary nucleus of medulla. ...
[Arai K et al; Brain Nerve Tokyo 38 (12): 1181-86 (1986)]**PEER REVIEWED**

Autopsy findings on a man who fell from a height due to acute **toluene** poisoning while painting are described. Gas chromatographic examination revealed that the **toluene** concentrations of his blood, lung, liver and brain were 48, 35, 65 and 80 ug/g, respectively. These **toluene** levels were not enough to be definitely lethal, but were enough to anesthetize the central nervous system.
[Takeichi S et al; Forensic Sci Int 32 (2): 109-16 (1986)]**PEER REVIEWED**

The psychological performance of 43 rotogravure printers exposed to a mean time- weighted average of 117 ppm **toluene** for a mean time period of 21.7 yr was compared to that of 31 offset printers with a mean working period of 23 yr. The offset printers were exposed to mixtures of aliphatic hydrocarbons or ethyl acetate (amounts not given) for a total of 10 to 60 min daily. Drinking habits were considered in grouping the workers. The test battery consisted of standardized tests for verbal and visual cognition and memory, perceptual motor speed, and psychomotor abilities. Performances of the two printer groups were similar with rotogravure printers having statistically significant lower scores on tests measuring visual cognitive abilities. Mean test performances indicated that drinking habits did not explain the impairment of visual cognitive abilities.
[Hanninen H et al; Int Arch Occupat Environ Health 59 (5): 475-83 (1987)]**PEER REVIEWED**

Acute poisoning may result from exposure to high concn of **toluene**; A /CNS depressant/ effect is produced. Human death has resulted from exposure to 10,000 ppm. **Toluene** is more acutely toxic than benzene; however, severe blood disorders of the type associated with benzene are not reported. Inhalation of 200 ppm has affected the CNS in humans.
[Cleland, J.G., G.L. Kingsbury. Multimedia Environmental Goals for Environmental Assessment. Volume 1. EPA-600/7-77-136a. Research Triangle Park, NC: EPA, Nov. 1977.,p. E-146]**PEER REVIEWED**

Vapors irritate eyes and upper respiratory tract; Cause dizziness, headache, anesthesia, and respiratory arrest. Liquid irritates eyes. If aspirated, causes coughing, gagging, distress, and rapidly developing pulmonary edema. If ingested causes vomiting, griping, diarrhea, and depressed respiration. Kidney and liver damage may follow ingestion.
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

In recent years some youngsters have been indulging in what is called thinner inhalation, posing a serious social problem. Organic solvents have also been widely used industrially as adhesives or degreasing and rinsing agents, generating a kind of occupational disease which has become a medical problem. Some

school children who refuse to go to school complaining of headache, head heaviness, blurred vision, diplopia, or dizziness, may actually have **toluene** toxicosis caused by the adhesive they use in constructing plastic models. /An examination of/ 35 such patients neurogically, found some impairment in the cerebellar cortex, cerebellar nuclei, or efferent pathways. This report is presented to invite comments from other researchers.
[Sakata E et al; Pract Otal Kyoto 79 (12): 1999-2013 (1986)]**PEER REVIEWED**

Severe, acute **toluene** intoxication in two workers was described. Special attention was paid to the metabolism of **toluene** in man and to the choice of reference parameters to monitor intoxication. The men had tiled a small swimming pool to be used for exercise programs in a rehabilitation clinic. They had used a special glue to make the joints of cement between the tiles resistant to bleaching solution; the next day they removed the excess glue using **toluene**. One worker was exposed for 2 hours and the other for 3 hours. Both were overcome with the fumes, and were found lying at the bottom of the pool. Symptoms included stupefaction, paresis, and amnesia. Patient-A had mucosal irritation of the eyes and slurred speech. He was stuporose and unable to walk or sit. His amnesia lasted for about 3 hours. Patient-B had mucosal irritation of the eyes, was drowsy, and was just able to walk. He had normal speech and complained of headache. The duration of his amnesia was about 2.5 hours. Solid evidence for **toluene** exposure was provided by the blood **toluene** concentration. The concentration 2 hours after exposure was 4.1 mg/l in patient-A and 2.2 mg/l in patient-B.
[Meulenbelt J et al; Br J Ind Med 47 (6): 417-20 (1990)]**PEER REVIEWED**

The memory sequelae for a group of female workers accidentally exposed to organic solvents were examined retrospectively to evaluate complaints of residual memory impairment. The subjects included seven employees (mean age 32.1 years) who agreed to retesting and who had been severely intoxicated by exposure to **toluene** and aliphatic hydrocarbons found in adhesives used in the manufacture of tennis balls. They were compared to eight workers (mean age 33.7 years) who were solvent exposed but not affected by the accident and ten workers (mean age 36.6 years) who had no exposure. Acute symptoms included faintness, nausea, vomiting, and headache. Complaints of impaired memory, personality changes, and loss of confidence persisted 8 months after exposure. Memory testing was first performed 2 months after exposure, with the follow up 6 months later to assess recovery. The three memory tasks included paired associate task, serial position task, and Brown-Peterson task. The subjects showed normal patterns of performance on tests of learning and short term and long term memory, but demonstrated marked difficulties when attention had to be divided between two resource competing tasks. The clearest evidence of impairment was observed in the Brown-Peterson task, where the acute group showed a significantly greater increase in word recall omission after periods of counting backwards in threes. The magnitude of the memory sequelae was not correlated with scores of self rated depression. It was concluded that solvent intoxication can cause neuropsychological sequelae lasting more than 8 months; memory tasks could prove useful in identifying memory impairment in other occupationally exposed groups.
[Stollery BT, Flindt MLH; Scand J Work, Environ, Health 14 (1): 45-8 (1988)]**PEER REVIEWED**

In a cross-sectional study of 181 male workers of a rotogravure printing plant, most of whom were exposed to **toluene** levels well above the GDR threshold limit values, 55 subjects revealed pathological liver screening values (activities of serum aspartate aminotransferase, alanine aminotransferase, gamma

glutamyltransferase; liver size). The differential diagnostic examination showed in 51 of these 55 subjects an association with competing factors such as alcohol abuse (78%) and overweight (40%), to a slight extent disorders of fat and carbohydrate metabolism and of the gallbladder. Drug intake did not play any role. The variance and regression analyses of the biochemical data have shown that alcohol significantly and considerably increases the activities of all three enzymes tested. Bodyweight had a similar, but less pronounced, significant effect. On the other hand, in subjects with a higher alcohol intake the activities of liver enzymes in highly **toluene** exposed subgroups were significantly and clearly lower than among slightly **toluene** exposed workers.
[Boewer C et al; Int Arch Occup Environ Health 60 (3): 181-6 (1988)]**PEER REVIEWED**

General health effects include lethality, growth, morbidity, liver and kidney damage and miscellaneous effects. Neurobehavioral effects include epidemiological and clinical findings, activity and sleep, performance and learning, electrophysiological effects. Evaluation and synthesis of data is included. It was concluded that low level exposure to **toluene** has its primary effect on the CNS. From a systematic or general point of view it is not clear what this effect is. Both depressant and excitatory effects (possibly concentration dependent) were reported as well as other kinds of results. Other health effects were not life threatening at any exposure level short of that producing lethality. Effects were reversible even at extremely high exposure levels for very long durations.
[Benignus VA; Neurotoxicol 2 (3): 567-88 (1981)]**PEER REVIEWED**

Toluene embryopathy is characterized by microcephaly, central nervous system dysfunction, attentional deficits and hyperactivity, developmental delay with greater language deficits, minor craniofacial and limb anomalies, and variable growth deficiency. Previously, three affected children, born to women who inhaled **toluene** regularly throughout pregnancy, have been reported. Two more cases are described emphasizing the importance of **toluene** as a potential human teratogen.
[Hersh JH; J Med Genet 26 (5): 333-7 (1989)]**PEER REVIEWED**

Neurobehavioral tests were undertaken by 30 female workers exposed to **toluene** and matched controls with low occupational exposure to **toluene**. The environmental air levels (TWA) of **toluene** was 88 ppm for the exposed workers and 13 ppm for the controls. The **toluene** in blood concentrations for the exposed workers was 1.25 mg/l and for the controls 0.16 mg/l. Statistically significant differences between workers exposed to **toluene** and controls in neurobehavioral tests measuring manual dexterity (grooved peg board), a visual scanning (trail making, visual reproduction, Benton visual retention, and digit symbol), and verbal memory (digit span) were observed. Further, the performance at each of these tests was related to time weighted average exposure concentrations of air **toluene**. The workers exposed to **toluene** had no clinical symptoms or signs. The question arises as to whether these impairments in neurobehavioral tests are reversible or whether they could be a forerunner of more severe damage.
[Foo SC et al; BR J Ind Med 47 (7): 480-4 (1990)]**PEER REVIEWED**

When compared with benzene, **toluene** has little to no effect on immunocompetence. However, it should be noted that **toluene** exposure effectively attenuates the immunotoxic effects of benzene (probably because of competition for metabolic enzymes).
[Klaassen, C.D., M.O. Amdur, Doull J. (eds.). Casarett and Doull's Toxicology. The Basic Science of Poisons. 5th ed. New York, NY: McGraw-Hill, 1995. 380]**PEER REVIEWED**

Neutral organic solvents such as ... **toluene** ... cause pain on contacting the eye, and examination after a generous splash of solvent shows dulling of the cornea. The epithelium will show punctate staining with fluorescein. The damage appears to be scattered loss of epithelial cells due to solution of some of the fats that occur in these cells.
[Klaassen, C.D., M.O. Amdur, Doull J. (eds.). Casarett and Doull's Toxicology. The Basic Science of Poisons. 5th ed. New York, NY: McGraw-Hill, 1995. 586]**PEER REVIEWED**

Toxicities associated with **toluene**: CNS depression, syncope, coma, cardiac arrhythmias and sudden death, ataxia, convulsions, rhabdomyolysis, increased creatine phosphokinase, abdominal pain, nausea, vomiting, hematemesis, peripheral neuropathy, paresthesias, encephalopathy, optic neuropathy, cerebella ataxia, distal renal tubular acidosis, hyperchloremia, hypokalemia, azotemia, hypophosphatemia, hematuria, proteinuria, pyruria, normalities, decreased cognitive function, fatal overdose. /From table/
[Ellenhorn, M.J., S. Schonwald, G. Ordog, J. Wasserberger. Ellenhorn's Medical Toxicology: Diagnosis and Treatment of Human Poisoning. 2nd ed. Baltimore, MD: Williams and Wilkins, 1997. 1494]**PEER REVIEWED**

Women workers exposed to high air concentrations of **toluene** (50-150 ppm) appeared to have a higher incidence of spontaneous abortion than a similar group of women with no occupational exposure to **toluene**.
[Ellenhorn, M.J., S. Schonwald, G. Ordog, J. Wasserberger. Ellenhorn's Medical Toxicology: Diagnosis and Treatment of Human Poisoning. 2nd ed. Baltimore, MD: Williams and Wilkins, 1997. 166]**PEER REVIEWED**

Maternal spray paint or glue sniffing leads to maternal complications including renal tubular acidosis, hypokalemia, hypocalcemia, cardiac arrhythmias, rhabdomyolysis, and premature labor. Premature **toluene** exposure leads to a characteristic pattern of anomalies similar to findings in infants exposed to alcohol in utero, consisting of an increased incidence of malformations, poor growth, and developmental delays.
[Ellenhorn, M.J., S. Schonwald, G. Ordog, J. Wasserberger. Ellenhorn's Medical Toxicology: Diagnosis and Treatment of Human Poisoning. 2nd ed. Baltimore, MD: Williams and Wilkins, 1997. 166]**PEER REVIEWED**

Eye and upper airway irritation occurred after a 6.5 hr exposure to an air level of 100 ppm (377 mg/cu m) **toluene**, and lachrymation was seen at 500 mg/cu m.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47 101 (1989)]**PEER REVIEWED**

Volunteers exposed to 100 ppm (377 mg/cu m) **toluene** for 6 hr/day for four days suffered from subjective complaints of headache, dizziness and a sensation of intoxication. In subjects exposed to 750 mg/cu m for 8 hr, fatigue, muscular weakness, confusion, impaired coordination, enlarged pupils and accommodation disturbances were experienced; at about 3000 mg/cu m, severe fatigue, pronounced nausea, mental confusion, considerable incoordination with staggering gait and strongly affected pupillary light reflexes were observed. After exposure at the high level, muscular fatigue, nervousness and insomnia lasted for several days. Heavy accidental exposure leads to coma.

[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47 101 (1989)]**PEER REVIEWED**

Humans exposed to concentrations of **toluene** of between 200-800 ppm may experience respiratory and ocular irritation.
[Sullivan, J.B. Jr., G.R. Krieger (eds.). Hazardous Materials Toxicology-Clinical Principles of Environmental Health. Baltimore, MD: Williams and Wilkins, 1992. 1090]**PEER REVIEWED**

Children with microcephaly, minor craniofacial and limb anomalies, central nervous system defects, attention disorders, developmental delay, learning disorders, and language deficits were born to mothers who abuse **toluene** by inhalation during pregnancy.
[Sullivan, J.B. Jr., G.R. Krieger (eds.). Hazardous Materials Toxicology-Clinical Principles of Environmental Health. Baltimore, MD: Williams and Wilkins, 1992. 1091]**PEER REVIEWED**

Controlled exposure effects on volunteers were studied at **toluene** concentrations ranging from 40, 60, or 100 ppm. ... Psychologic measurements indicated decrements in vigilance, visual perception, motor performance, and ability to carry out functions at 100 ppm.
[Sullivan, J.B. Jr., G.R. Krieger (eds.). Hazardous Materials Toxicology-Clinical Principles of Environmental Health. Baltimore, MD: Williams and Wilkins, 1992. 1092]**PEER REVIEWED**

Acute effects in humans following exposure to **toluene**: 50-100 ppm: subjective complaints (fatigue or headache), but probably no observable impairment of reaction time or coordination; 200 ppm: mild throat and eye irritation; 100-300 ppm: detectable signs of incoordination may be expected during exposure periods up to 8 hr; 400 ppm: lacrimation and irritation to the eyes and throat; 300-800 ppm: gross signs of incoordination may be expected during exposure periods up to 8 hr; 1500 ppm: probably not lethal for exposure periods of up to 8 hr; 4000 ppm: would probably cause rapid impairment of reaction time and coordination, exposures of one hr or longer might lead to /CNS depression/ and possibly death; 10,000-30,000 ppm: onset of /CNS depression/ within a few minutes, longer exposures may be lethal. /From table/
[Zenz, C., O.B. Dickerson, E.P. Horvath. Occupational Medicine. 3rd ed. St. Louis, MO., 1994 724]**PEER REVIEWED**

Studies of women exposed to solvents such as benzene, **toluene**, and xylene have shown menstrual disturbances, principally associated with abnormal bleeding.
[Rom, W.N. (ed.). Environmental and Occupational Medicine. 2nd ed. Boston, MA: Little, Brown and Company, 1992. 155]**PEER REVIEWED**

FROM THE STANDPOINT OF CHRONIC EXPOSURE, IT IS CLEAR THAT **TOLUENE** DOES NOT CAUSE THE SEVERE INJURY TO THE BONE MARROW THAT IS CHARACTERISTIC OF BENZENE POISONING.
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Volumes I,II, III. Cincinnati, OH: ACGIH, 1991.

1571]**PEER REVIEWED**

Toluene abuse (to 10,000 ppm) has been linked with kidney disease as evidenced by blood (hematuria), protein (proteinuria), albumin (albuminuria), and pus (pyuria) in the urine, accompanied by elevated serum creatinine, decreased urinary output, and metabolic and renal tubular acidosis.
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Volumes I,II, III. Cincinnati, OH: ACGIH, 1991.
1573]**PEER REVIEWED**

... The highest **toluene** concentrations in air that could be tolerated for 3.5-6 hr without measurable decrements on behavioral test performance were 80 ppm to 100 ppm.
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Volumes I,II, III. Cincinnati, OH: ACGIH, 1991.
1574]**PEER REVIEWED**

The pregnancies of four of five women associated with gross **toluene** abuse (0.5 to 2 cans of spray paint/day for 6 mos to 11 yr) resulted in evidence of renal toxicity (as evidenced by severe renal tubular acidosis), fetal toxicity (manifest as intrauterine growth retardation), and teratogenicity (deformed external ears, ventricular septal defect, micrognathia, hydronephrosis) with facial features reminiscent of the FAS (short palpebral fissures, epicanthal folds, maxillary hypoplasia).
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Volumes I,II, III. Cincinnati, OH: ACGIH, 1991.
1575]**PEER REVIEWED**

In a case study of two adult white males who suffered from **toluene** intoxication while removing glue from tiles in a swimming pool, cardiac arrhythmias were noted. Response seemed to be highly variable among individuals. One person exposed for 2 hr to less than 1890 ppm **toluene** exhibited a rapid heartbeat (sinus tachycardia), while the second person, exposed for 3 hr, exhibited a slow heartbeat (bradycardia).
[Meulenbelt J et al; Br J Ind Med 47: 417-20 (1990) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.31 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

Severe renal tubular acidosis was observed in five pregnant women who were chronic abusers of paints containing **toluene**.
[Goodwin TM; Obstet Gynecol 71: 715-18 (1988) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.36 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

Exposure of students to 75 or 150 ppm **toluene** for 7 hr caused a dose-related impairment of function on digit span, pattern recognition, the one hole test, and pattern memory. There was an effect on the results of the symbol digit test but the effect was not dose related. Subjects served as their own controls. ... There were no differences in the results on simple reaction time, POMS mood scale, visual memory,

hand-eye coordination, Sternberg test, finger tapping, reaction time, continuous performance test, and critical tracking test.
[Echeverria D et al; Br J Ind Med 48: 750-61 (1991) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.40 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

A group of 95-104 workers exposed to TWA of 41-46 ppm **toluene** during shoemaking, printing, and audio equipment production were evaluated for symptoms and signs of exposure when compared to 130 control subjects. The incidence of health-related complaints among the **toluene** exposed workers was two to three times that of the controls. Dizziness was reported by about two-thirds of the **toluene** exposed respondents. These subjects also complained of headaches, sore throats, eye irritation, and difficulty with sleep. When the exposed subjects were divided into two groups, one with TWA exposures of less than 40 ppm and the other with exposures greater than or equal to 40 ppm, the incidence of headache and sore throat, but not dizziness, showed a dose-response pattern.
[Yin S et al; Ind Health 25: 113-30 (1987) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.41 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

Children born to **toluene** abusers have exhibited renal tubular acidosis immediately after birth due to hyperchloremia. In each incident the acidosis was resolved within 3 days of birth.
[Lindemann R; Acta Pediatr Scand 80: 882-4 (1991) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.49 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

Several case series have demonstrated that high exposure to **toluene** through sniffing during pregnancy induces a syndrome that closely resembles the fetal alcohol syndrome, with pre- and postnatal growth deficiency, microcephaly and developmental delay, typical craniofacial features including micrognathia, small palpebral fissures, and ear anomalies.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V71 845 (1999)]**PEER REVIEWED**

Renal tubular acidosis is one of a number of human complications reported in the offspring of mothers inhaling **toluene** during pregnancy. This article reports a case of a premature newborn with renal tubular acidosis probably due to maternal sniffing of paint containing **toluene**. Characteristics of this condition are described as well as its medical management.
[Erramouspe J et al; J Psychoactive Drugs 28 (2): 201-4 (1996)]**PEER REVIEWED**

Skin, Eye and Respiratory Irritations:

A human eye irritant. An experimental skin and severe eye irritant.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996.

3190]**PEER REVIEWED**

Medical Surveillance:

Yearly physical examinations of exposed personnel, with special attention to the eyes and central nervous system, including complete blood count and liver function tests.
[ITII. Toxic and Hazardous Industrial Chemicals Safety Manual. Tokyo, Japan: The International Technical Information Institute, 1988. 526]**PEER REVIEWED**

The clinical examination should include hemocytometric testing and a thrombocyte (platelet) count in view of the possibility that **toluene** may contain a certain proportion of benzene.
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 2185]**PEER REVIEWED**

Hippuric acid levels above 5 g/l of urine may result from exposure greater than 200 ppm determined as a time weighted average.
[Sittig, M. Handbook of Toxic and Hazardous Chemicals and Carcinogens, 1985. 2nd ed. Park Ridge, NJ: Noyes Data Corporation, 1985. 870]**PEER REVIEWED**

Populations at Special Risk:

Preclude individuals from exposure to **toluene** who have central nervous system or liver diseases.
[ITII. Toxic and Hazardous Industrial Chemicals Safety Manual. Tokyo, Japan: The International Technical Information Institute, 1988. 526]**PEER REVIEWED**

Probable Routes of Human Exposure:

NIOSH (NOES Survey 1981-1983) has statistically estimated that 1,625,598 workers (288,299 of these are female) are potentially exposed to **toluene** in the US(1). Occupational exposure to **toluene** may occur through inhalation and dermal contact with this compound at workplaces where **toluene** is produced or used(SRC). The general population may be exposed to **toluene** via inhalation of ambient air, ingestion of food and drinking water, handling of gasoline, and exposure to some consumer products where **toluene** is used as a solvent(SRC).
[(1) NIOSH; National Occupational Exposure Survey (NOES) (1983)]**PEER REVIEWED**

Toluene was detected in hairdresser salons in Norway at concns of 0.04-0.11 mg/cu m(1). The time weighted average (TWA) of **toluene** in the workplace air of a municipal waste composting facility was reported as 188,000 ug/cu m(2). In a 1989 Danish survey on chemical exposures(3), the number of worker exposure events for **toluene** were documented: manufacturing of metals, 420; manufacturing of metal fabricated products 64,000; electrical machinery and apparatus, 1,500; manufacture of transport equipment 2,700; painters and carpenters 15,000; construction workers, 5,400; publishing and printing, 6,300; wholesale trades, 5,000; textile and leather manufacturing, 4,400; wood and furniture manufacturing, 5,900; manufacture of chemicals, 8,700; manufacture of paints and petroleum, 1,400; manufacture of non-metallic mineral products, 2,300; manufacture of optical instruments, 2,500

manufacture of plastic and boat building, 1,100; sewage and refuse disposal, 99; agriculture and forestry, 11,000; health services, 2,600. The total number of work related exposure events was 140,000(3). **Toluene** was detected in the workplace air of glass fiber manufacturing plants and high temperature sealing component and clutch lining plants at a mean concn of 65 ppm(4).
[(1) Hollund BE, Moen BE; Ann Occup Hyg 42: 277-81 (1998) (2) Eitzer BD; Environ Sci Technol 29: 896-902 (1995) (3) Brandorff NP et al; Occup Environ Med 52: 454-63 (1995) (4) Angerer J, Kraemer A; Int Arch Occup Environ Health 69: 91-96 (1997)]**PEER REVIEWED**

Body Burden:

Toluene was identified, not quantified, in 8 samples of mothers' milk from 4 urban areas(1). **Toluene** was detected in 250 of 250 specimens of human blood at concns of 0.2-38 ppb (1.5 ppb avg)(2). **Toluene** was detected in 91% of the samples of the National Human Adipose Tissue Survey at a max concn of 250 ppb(3). **Toluene** was identified, not quantified, in expired breath of people at service stations during fueling(4). The mean concn of **toluene** in the blood of non-occupationally exposed individuals in the US was 0.52 ppb(5). The avg concn of **toluene** in the blood and urine of workers in glass fiber and clutch lining plants were 911 ug/l and 2.9 mg/l, respectively(6).
[(1) Pellizzari ED et al; Bull Environ Contam Toxicol 28: 322-8 (1982) (2) Antoine SR et al; Bull Environ Contam Toxicol 36: 364-71 (1986) (3) Stanley JS; Broad Scan Analysis of the FY82 National Human Adipose Tissue Survey Specimens Vol. I Executive Summary p. 5 USEPA-560/5-86-035 (1986) (4) Lindstrom AB, Pleil J; J Air Waste Manage Assoc 46: 676-82 (1996) (5) Ashley DL et al; Clin Chem 40: 1401-14 (1994) (6) Angerer J, Kraemer A; Int Arch Occup Environ Health 69: 91-96 (1997)]**PEER REVIEWED**

Average Daily Intake:

AIR INTAKE (assume median concn 11 ppb(1)) 843 ug; WATER INTAKE (assume 2 ppb(2)) 4 ug; FOOD INTAKE - insufficient data.
[(1) Brodzinsky R, Singh HB; Volatile Organics in the Atmosphere and Assessment of available data: p. 126-7 SRI Contract 68-02-3459 (1982) (2) Otson R et al; J Assoc Off Analyt Chem 65: 1370-4 (1982)]**PEER REVIEWED**

Minimum Fatal Dose Level:

Ingestion of approximately 60 ml (625 mg/kg) of **toluene** proved fatal for a while male mental patient.
[Ameno K et al; Forensic Sci Int 41: 255-60 (1989) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.52 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

Emergency Medical Treatment:

Emergency Medical Treatment:

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The following Overview, *** **TOLUENE** ***, is relevant for this HSDB record chemical.

Life Support:

- This overview assumes that basic life support measures have been instituted.

Clinical Effects:

SUMMARY OF EXPOSURE

0.2.1.1 ACUTE EXPOSURE

- ACUTE INGESTION -
  1. Causes CNS depression, oropharyngeal and gastric pain, vomiting.
- ACUTE INHALATION -
  1. Causes CNS excitation followed by CNS depression and nausea. Ataxia, fatigue, seizures and general anesthesia occur at high concentrations.
- CHRONIC INHALATION -
  1. SYNDROMES - Muscular weakness, gastroenteritis, renal tubular acidosis, and neuropsychiatric syndrome are common in **toluene** sniffers.
  2. EFFECTS - may include hypokalemia, hematuria, proteinuria, oliguria, paresis, rhabdomyolysis, hallucinations, hyperactive reflexes, peripheral neuropathy, personality changes, tremors, headaches, emotional lability, memory loss.
  3. SEQUELAE - Progressive, irreversible encephalopathy with cognitive difficulty and cerebellar ataxia, and organic affective syndromes have been described.
- EYE EXPOSURE -
  1. Blepharospasm, conjunctivitis, corneal edema, and corneal abrasions usually resolve over 1-2 days.
- DERMAL EXPOSURE -
  1. Prolonged or repeated dermal exposure to the liquid may defat the skin.

VITAL SIGNS

0.2.3.1 ACUTE EXPOSURE

- Bradycardia, hypotension and hypoventilation are rare effects.

HEENT

0.2.4.1 ACUTE EXPOSURE

- Eye exposure causes irritation and superficial injury. Chronic abuse associated with decreased visual acuity, impaired color vision, optic atrophy, and ototoxicity.

CARDIOVASCULAR

0.2.5.1 ACUTE EXPOSURE

- ACUTE INHALATION - may cause dysrhythmias (usually in chronic abusers). Bradycardia, ventricular fibrillation, and myocardial infarction have been reported.
- CHRONIC INHALATION - Chronic sniffers may develop dysrhythmias, including PVCs and supraventricular tachycardia; dilated cardiomyopathy has been reported.
- ACUTE INGESTION may cause tachycardia and hypertension.

RESPIRATORY

0.2.6.1 ACUTE EXPOSURE

- Inhalation may cause irritation, acute bronchitis, bronchospasm, pulmonary edema, pneumonitis, and asphyxia. Chronic abusers may develop respiratory failure.

NEUROLOGIC

0.2.7.1 ACUTE EXPOSURE

- ACUTE INGESTION - **Toluene** ingestion causes CNS depression.
- ACUTE INHALATION - 400 to 800 ppm: Euphoria, giddiness, tremors, nervousness, insomnia, headache, dizziness, fatigue, drowsiness, confusion, vertigo, increased reaction time; 800 ppm: ataxia, fatigue, seizures. 10,000 ppm: general anesthesia.
- CHRONIC INHALATION may cause hyperactive reflexes, peripheral neuropathy, personality changes, tremors, headaches, emotional lability, cognitive dysfunction, memory loss.

GASTROINTESTINAL

0.2.8.1 ACUTE EXPOSURE

- Ingestion or inhalation may cause vomiting, abdominal cramps, and diarrhea.

HEPATIC

0.2.9.1 ACUTE EXPOSURE

- Rarely hepatorenal failure has been attributed to **toluene** abuse or occupational exposure. Hepatomegaly and impaired liver function has also been reported.

GENITOURINARY

0.2.10.1 ACUTE EXPOSURE

- Transient distal renal tubular acidosis (RTA), with

hyperchloremic metabolic acidosis, hypokalemia, and urine pH >5.5, is common in hospitalized paint sniffers. negative.
- Proximal RTA or Fanconi's syndrome is less common (urine pH >5.5, uricosuria, hypophosphatemia, hypocalcemia).
- Isolated cases of irreversible renal insufficiency, glomerulonephritis, focal segmental glomerulosclerosis, acute interstitial nephritis, and renal failure secondary to myoglobinuria have been reported.

ACID-BASE

0.2.11.1 ACUTE EXPOSURE

- Hyperchloremic metabolic acidosis common in hospitalized **toluene** abusers.

FLUID-ELECTROLYTE

0.2.12.1 ACUTE EXPOSURE

- Hypokalemia, metabolic acidosis, and hypophosphatemia are typical; hypercalcemia and hypouricemia less frequent. Hypocalcemia and precipitation of tetany has occurred during correction of acidemia.
- Patients with weakness may have severe fluid/electrolyte imbalance.

DERMATOLOGIC

0.2.14.1 ACUTE EXPOSURE

- Prolonged contact may cause drying and defatting or superficial burns.

MUSCULOSKELETAL

0.2.15.1 ACUTE EXPOSURE

- Rhabdomyolysis is common in chronic **toluene** abusers. Severe muscle weakness is a common presentation in chronic abuse.

PSYCHIATRIC

0.2.18.1 ACUTE EXPOSURE

- Psychiatric disorders are common in chronic **toluene** abusers; including bizarre behavior, acute paranoid psychosis, confusion, visual and auditory hallucinations, mood lability, and decreased IQ.

REPRODUCTIVE HAZARDS

- Multiple physical deformities, with signs similar to fetal alcohol syndrome, microencephaly, CNS dysfunction, and variable growth deficiencies have occurred in infants born to mothers who abused **toluene** during pregnancy.

GENOTOXICITY

- There is conflicting information in the literature regarding the potential of **toluene** to cause DNA strand

breaks. **Toluene** was not mutagenic in the Ames assay. Chromosome damage has been reported.

Laboratory:

- **Toluene** may be measured in the breath and blood; hippuric acid and cresol metabolites may be measured in the urine.
- Obtain a baseline CBC and monitor renal and hepatic function tests, urinalysis (including urine pH) electrolytes, and CPK. Monitor arterial blood gases in symptomatic patients.

Treatment Overview:

ORAL EXPOSURE

- EMESIS - Emesis is probably not indicated due to the possibility for aspiration of gastric contents.
- GASTRIC LAVAGE may be indicated when the patient has ingested a large quantity of **toluene**, or there is a large amount of benzene contamination, and emesis is contraindicated (obtunded, comatose, convulsing). The potential toxicity of the amount ingested must be weighed against the substantial risk of aspiration.

1. GASTRIC LAVAGE: Consider after ingestion of a potentially life-threatening amount of poison if it can be performed soon after ingestion (generally within 1 hour). Protect airway by placement in Trendelenburg and left lateral decubitus position or by endotracheal intubation. Control any seizures first.

a. CONTRAINDICATIONS: Loss of airway protective reflexes or decreased level of consciousness in unintubated patients; following ingestion of corrosives; hydrocarbons (high aspiration potential); patients at risk of hemorrhage or gastrointestinal perforation; and trivial or non-toxic ingestion.

- ACTIVATED CHARCOAL: Administer charcoal as slurry (240 mL water/30 g charcoal). Usual dose: 25 to 100 g in adults/adolescents, 25 to 50 g in children (1 to 12 years), and 1 g/kg in infants less than 1 year old.
- MONITOR FLUID and ELECTROLYTE STATUS CAREFULLY. Correct hypokalemia with intravenous potassium.
- MONITOR PATIENT for RESPIRATORY DISTRESS.
- MONITOR EKG and VITAL SIGNS REGULARLY. Use epinephrine cautiously if indicated.
- CHRONIC EXPOSURE - Evaluate renal and liver function.

INHALATION EXPOSURE

- DECONTAMINATION: Move patient to fresh air. Monitor

for respiratory distress. If cough or difficulty in breathing develops, evaluate for respiratory tract irritation, bronchitis, or pneumonitis. Administer 100 percent humidified supplemental oxygen with assisted ventilation as required.
- MONITOR FLUID and ELECTROLYTE STATUS CAREFULLY. Correct hypokalemia with potassium. CAUTION - Hypocalcemia may ensue following fluid and electrolyte replenishment.
- MONITOR for RESPIRATORY DISTRESS, assure airway patency and adequacy of ventilation and oxygenation.
- MONITOR EKG and VITAL SIGNS REGULARLY. Use epinephrine cautiously if indicated.

EYE EXPOSURE
- DECONTAMINATION: Exposed eyes should be irrigated with copious amounts of tepid water for at least 15 minutes. If irritation, pain, swelling, lacrimation, or photophobia persist, the patient should be seen in a health care facility.

DERMAL EXPOSURE
- DECONTAMINATION: Wash exposed area extremely thoroughly with soap and water. A physician may need to examine the area if irritation or pain persists.

Range of Toxicity:

- Ingestion - 60 mL lethal in an adult. Inhalation - 600 to 800 ppm for 3 hrs caused fatigue, nausea, confusion, ataxia; 10,000 ppm causes general anesthesia.

[Rumack BH: POISINDEX(R) Information System. Micromedex, Inc., Englewood, CO, 2001; CCIS Volume 107, edition exp February, 2001. Hall AH & Rumack BH (Eds):TOMES(R) Information System. Micromedex, Inc., Englewood, CO, 2001; CCIS Volume 107, edition exp February, 2001.]
PEER REVIEWED

Antidote and Emergency Treatment:

Basic treatment: Establish a patent airway. Suction if necessary. Watch for signs of respiratory insufficiency and assist ventilations if necessary. Administer oxygen by nonrebreather mask at 10 to 15 L/min. Monitor for pulmonary edema and treat if necessary ... . Monitor for shock and treat if necessary ... . For eye contamination, flush eyes immediately with water. Irrigate each eye continuously with normal saline during transport ... . Do not use emetics. For ingestion, rinse mouth and administer 5 ml/kg up to 200 ml of water for dilution if the patient can swallow, has a strong gag reflex, and does not drool. Administer activated charcoal ... . /Aromatic hydrocarbons and related compounds/
[Bronstein, A.C., P.L. Currance; Emergency Care for Hazardous Materials Exposure. 2nd ed. St. Louis, MO. Mosby Lifeline. 1994.,p.

181-2]**PEER REVIEWED**

Advanced treatment: Consider orotracheal or nasotracheal intubation for airway control in the patient who is unconscious or in respiratory arrest. Positive-pressure ventilation techniques with a bag-valve-mask device may be beneficial. Monitor cardiac rhythm and treat arrhythmias if necessary ... . Start an IV with D5W /SRP: "To keep open", minimal flow rate/. Use lactated Ringer's if signs of hypovolemia are present. Watch for signs of fluid overload. Consider drug therapy for pulmonary edema ... . Treat seizures with diazepam (Valium) ... . Use proparacaine hydrochloride to assist eye irrigation ... . /Aromatics hydrocarbons and related compounds/
[Bronstein, A.C., P.L. Currance; Emergency Care for Hazardous Materials Exposure. 2nd ed. St. Louis, MO. Mosby Lifeline. 1994. 182]**PEER REVIEWED**

Animal Toxicity Studies:

Evidence for Carcinogenicity:

Evaluation: There is inadequate evidence for the carcinogenicity of **toluene** in humans. There is evidence suggesting lack of carcinogenicity of **toluene** in experimental animals. Overall evaluation: **Toluene** is not classifiable as to its carcinogenicity to humans (Group 3).
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V71 855 (1999)]**PEER REVIEWED**

CLASSIFICATION: D; not classifiable as to human carcinogenicity. BASIS FOR CLASSIFICATION: No human data and inadequate animal data. **Toluene** did not produce positive results in the majority of genotoxic assays. HUMAN CARCINOGENICITY DATA: None.
[U.S. Environmental Protection Agency's Integrated Risk Information System (IRIS) on Toluene (108-88-3) Available from: http://www.epa.gov/ngispgm3/iris on the Substance File List as of March 15, 2000]**PEER REVIEWED**

A4. A4= Not classifiable as a human carcinogen.
[American Conference of Governmental Industrial Hygienists. TLVs and BEIs. Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. Cincinnati, OH. 2000. 67]**QC REVIEWED**

Non-Human Toxicity Excerpts:

A TEMPORARY INCOORDINATION WITH MUSCULAR TREMORS HAS BEEN OBSERVED IN PUPPIES & KITTENS & IN DOGS AT TWICE THERAPEUTIC DOSE LEVEL. CALVES IN POOR CONDITION SHOWED STAGGERING GAIT AND SOME COLLAPSED BUT RECOVERY WAS COMPLETE AFTER UP TO 4 HOURS. FOUR TIMES THERAPEUTIC DOSE RATE PRODUCED NO OBSERVABLE CHANGES IN ... ORGANS.
[Clarke, M. L., D. G. Harvey and D. J. Humphreys. Veterinary Toxicology. 2nd ed. London: Bailliere Tindall, 1981. 100]**PEER

REVIEWED**

... /CNS DEPRESSANT/ EFFECT OF **TOLUENE** ... IS EXERTED IN 2 PHASES--A PRELIMINARY ... /CNS DEPRESSION/ FOLLOWED BY STAGE OF EXCITEMENT, MANIFESTED BY TREMOR, MUSCULAR CRAMPS AND DISTURBANCES IN BEHAVIOR ...
[Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965. 70]**PEER REVIEWED**

... SWELLING OF GLOMERULI, CYLINDERS & ALBUMIN IN URINE IN 2 ... DOGS. BUT ... /INVESTIGATORS/ NOTE THAT THE DOGS WERE OF BREED WHICH FREQUENTLY DEVELOP INTERSTITIAL NEPHRITIS. ... HEMORRHAGIC & DEGENERATIVE LESIONS IN GOATS.
[Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965. 72]**PEER REVIEWED**

IN DOGS ... CONGESTION & HEMORRHAGIC FOCI WERE PRESENT IN LIVER; THESE LESIONS ... ALSO PRESENT IN GOATS ... CONGESTION & SOME ALVEOLAR INFLAMMATION /OF LUNG ALSO/ ... IN DOGS & ... GOATS. SPLEEN ... SHOWED SOME DIMINUTION OF LYMPHOID FOLLICLES & PLAQUES OF HEMOSIDEROSIS.
[Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965. 71]**PEER REVIEWED**

EFFECTS IN CATS EXPOSED TO 7800 PPM (31.0 MG/L)/6 HR: CNS EFFECTS, MYDRIASIS, MILD TREMORS, PROSTRATION IN 80 MIN, LIGHT ANESTHESIA IN 2 HR. /FROM TABLE/
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1327]**PEER REVIEWED**

INTRATRACHEAL ADMIN /TO CATS/ WITH CHRONICALLY IMPLANTED ELECTRODES INDUCED SEIZURES ALONG WITH BEHAVIORAL DISTURBANCES SUCH AS NODDING, TWITCHING & APPARENT HALLUCINATIONS.
[CONTRERAS CM ET AL; ELECTROENCEPHALOGR CLIN NEUROPHYSIOL 46 (3): 290 (1979)]**PEER REVIEWED**

... RATS /EXPOSED/ TO 1500 MG/CU M OF AIR FROM DAY 1 THROUGH 8 OR 1000 MG/CU M FOR 8 HR DAILY FROM DAY 1 THROUGH DAY 21 /OF GESTATION/ ... /WITH/ NO TERATOGENIC EFFECT. SOME FETAL GROWTH RETARDATION ... @ HIGHER DOSE ... MICE WERE EXPOSED DURING DAYS 6-13 TO 1500 MG/CU M OF AIR WITH SIMILAR RESULTS.
[Shepard, T.H. Catalog of Teratogenic Agents. 5th ed. Baltimore, MD: The Johns Hopkins University Press, 1986. 1438]**PEER REVIEWED**

/GAVAGING/ MICE /WITH/ 1.0 MG/KG ON DAYS 6 THROUGH 15 /OF GESTATION/ ... INCR CLEFT PALATE IN THE OFF-SPRING.
[Shepard, T.H. Catalog of Teratogenic Agents. 5th ed. Baltimore, MD: The Johns Hopkins University Press, 1986. 1438]**PEER REVIEWED**

TOLUENE WAS UNABLE TO REVERT SALMONELLA TYPHIMURIUM STRAINS TA1535, TA1537, TA1538, TA98 AND TA100 IN THE AMES SALMONELLA/MICROSOME ASSAY,

EITHER WITH OR WITHOUT METABOLIC ACTIVATION BY S9 MIX FROM LIVERS OF RATS EITHER UNTREATED OR INDUCED WITH AROCLOR 1254.
[BOS RP ET AL; MUTAT RES 88: 273 (1981)]**PEER REVIEWED**

FOLLOWING IP ADMIN OF 1 ML **TOLUENE**/KG DAILY FOR 21 DAYS TO RATS, MIXED-FUNCTION OXYGENASE ACTIVITY INCREASED 33.8% IN LIVER BUT WAS UNCHANGED IN BRAIN.
[CHAND P, CLAUSEN J; BULL ENVIRON CONTAM TOXICOL 28 (5): 542 (1982)]**PEER REVIEWED**

TOLUENE & M-XYLENE CAUSED MUSCULAR WEAKNESS & EQUILIBRIUM DISTURBANCES IN THE RAT FOLLOWING IP ADMIN. THE LOCOMOTOR (OPEN-FIELD BEHAVIOR) & RUNNING ACTIVITY (WHEEL-RUNNING) IN THE RAT WAS MOST AFFECTED BY **TOLUENE**. THESE DIFFERENCES WERE RELATED TO THE DIFFERENCES IN THE STIMULATORY EFFECTS OF THE SOLVENTS ON THE CNS.
[PAKSY KA ET AL; ACTA PHYSIOL ACAD SCI HUNG 59 (4): 317 (1982)]**PEER REVIEWED**

RATS WERE EXPOSED TO **TOLUENE** OR N-HEXANE OR A MIXT OF THE 2 CMPD AT 1000-8000 PPM FOR 8 HR. ACETYLCHOLINE WAS INCR AT LOW CONCN OF THE SOLVENTS, BUT WAS GREATLY DECR AT HIGH CONCN. CHOLINE ACETYLTRANSFERASE WAS DECR SIGNIFICANTLY AT HIGH CONCN OF THE MIXT. ACETYLCHOLINE ESTERASE ACTIVITY WAS INCR BY THE SOLVENTS.
[HONMA T; TOXICOL LETT 16 (1-2): 17 (1983)]**PEER REVIEWED**

In skin painting studies with CF1, CH, and BaH strains of mice, 0.05 to 0.1 ml/mouse was applied to 25 mice/sex/strain for 52 weeks. Results were negative for tumor development.
[USEPA; Ambient Water Quality Criteria Doc: Toluene p.C-26 (1980) EPA 440/5-80-075]**PEER REVIEWED**

Intraperitoneal admin of 250, 500, or 1,000 mg/kg at 0 and 24 hr failed to give positive results in micronucleus test with Swiss mice.
[USEPA; Ambient Water Quality Criteria Doc: Toluene p.14-6 (1980) EPA 440/5-80-075]**PEER REVIEWED**

... Groups of rats were trained on the conditioned avoidance response task during the last week of a 5 week exposure to 1400 or 1200 ppm **toluene** (14 hr/day, 7 days/week) or during the first or third weeks after the exposure ended. None of the three groups ... were able to acquire the auditory condition avoidance response ... . Subsequent tests ... revealed that hearing with these rats was unimpaired at 4 KHz, slightly impaired at 8 KHz, and markedly impaired at 12 KHz and above.
[Pryor GT et al; Neurobehav Toxicol Terat 5 (1): 53-7 (1983)]**PEER REVIEWED**

Pregnant CD-1 mice were housed singly in multicompartment cages in inhalation chambers and exposed to **toluene** at a concentration of 0, 750, or 1500 mg/cu m (0, 200, or 400 ppm) for 7 hrs/day from day 7 through day 16 of gestation. The mice were killed on day 17 of gestation and the fetuses were removed and examined. Maternal weight gain was not affected by **toluene** exposure but the liver to body weight ratio was significantly reduced. The treated dams showed no significant differences in the average

number of implantation sites, number of live fetuses, fetal mortality, or fetal body weight at either **toluene** concentration compared to control values. The incidence of enlarged renal pelvis was significantly greater in fetuses exposed to 200 ppm than in the fetuses exposed to 400 ppm or in the controls. A shift in rib profile (number of fetuses with 13 ribs) was observed in the higher **toluene** concentration group, and this shift was significantly different from the rib profile of controls. There was an increase in the total activity of lactic dehydrogenase activity in the brain of the dams from the 400 ppm group. The total activity of lactic dehydrogenase in the **toluene** exposed pups did not differ significantly from the controls for liver, heart, lung, or kidney, but the brain lactic dehydrogenase activity of the treated group was slightly greater than the control value.
[Courtney KD et al; Fundam Appl Toxicol 6: 145-54 (1986)]**PEER REVIEWED**

Behavioral toxicity of **toluene** was assessed in mice confined in a 20 liter hermetically sealed chamber for several hours. **Toluene** was introduced through a port and volatilized by a hot plate. Samples of chamber air for analysis were taken through another port. A smaller mesh cage held the mouse within the larger chamber. Schedule-controlled responding was developed by arranging that a response, breaking a beam of light, was followed by mild (under an F1 60 sec) schedule. Responding was much more rapid in the presence of stimuli correlated with the F1 schedule than when the schedule was not operating. Standard sessions consisted of alternating series of 8 consecutive F1 60 sec and inter-series 30 min time-outs. Concentration-effect curves were determined by exposing a mouse to incremental additions of **toluene** at 30 min intervals. **Toluene** increased the rate of responding in most mice at levels of about 700 ppm. Higher concentrations progressively reduced responding. The ED50 (the concentration reducing responding by 50%) averaged 1657 ppm in 10 mice. It is estimated that there is a 1/1000 chance /ED001/ of the responding of a mouse being reduced by as much as 10% by a concentration of **toluene** of 69 ppm.
[Glowa JR et al; J Environ Pathol Toxicol Oncol 6 (5-6): 153-68 (1986)]**PEER REVIEWED**

Sixteen rats were chronically implanted with bipolar electrodes in the hipocampal regions containing cells generating electric theta-activity. The animals were divided into 4 groups of which 2 were exposed to 500 ppm of **toluene** in inhalation chambers, for 8 or 16 hours per day for 5 days per week in 12 weeks respectively, and 2 served as controls. The hippocampal electric activity was recorded 48 hours after each weekly exposure. Frequencies of theta-activity in the exposed groups were found to differ from their respective control group by variance analysis. Each point on the frequency versus time plot were further analysed by Student's t-test. Compared to the non-exposed group the eight hours daily exposed showed an initial period of increased frequency of the regular theta-waves together with an increased incidence of theta-activity after 1-2 weeks of exposure. In the sixteen hours daily exposed rats two weeks of **toluene** inhalation produced a significant reduction in the theta-wave frequency. This change was also reached after either weeks of exposure in the eight hours daily exposed group. At this moment the theta-activity was frequency disrupted by short amplitude irregular waves, a phenomen which increased gradually throughout the rest of the exposure period. The average blood concentration of **toluene** was 16.7 ug/ml and 17.7 ug/ml and not significantly different for the eight and sixteen hours exposed groups respectively.
[Naalsund LU; Acta Pharmacol Toxicol 59 (4): 325-31 (1988)]**PEER REVIEWED**

The effects of **toluene** vapors on brain lipid changes were investigated in male Sprague-Dawley rats. The animals (8/group) were continuously exposed to 320 ppm **toluene** for 30 days. Controls were exposed to

air. Exposed animals showed decreased body weight ($p< 0.01$), decreased brain weight ($p< 0.01$), and a decrease in the weight of the cerebral cortex ($p< 0.05$) when compared to controls. In the cerebral cortex of exposed rats, total phospholipids was reduced ($p< 0.001$), there was an increase in phosphatidic acid ($p< 0.05$) and a decrease in a minor fatty acid of ethanolamine phosphoglyceride ($p< 0.05$). No changes in lipids were found in the brain stem.
[Kyrklund T et al; Toxicology 45: 123-33 (1987)]**PEER REVIEWED**

With the intention of investigating possible morphological alterations effected by **toluene** in the developing CNS, rat pups were exposed to 100 ppm and 500 ppm of atmospheric **toluene** from postnatal day 1 until sacrifice at postnatal day 28, when the hippocampal region (area dentata, Ammon's horn, subiculum) was examined by light microscope and alterations in the volumes of the layers of the subdivisions were determined. The layers of Ammon's horn and the subiculum were not affected qualitatively or quantitatively by the 500 ppm exposure. Within the area dentata, the volume of the granule cell layer was 6% smaller in animals exposed to 100 ppm and 13% smaller in animals exposed to 500 ppm than they were in controls. The volumes of the hilus, which is a terminal field of granule cell axons, and the commissural-association zone of the dentate molecular layer, which is the terminal field of the hilar projection to the granule cells, were smaller (12% and 19%) in animals exposed to 500 ppm than they were in controls. Argyrophilic cells were found in the granule cell layer of all animals exposed to 500 ppm. Pronounced granule cell degeneration was found in one animal exposed to 500 ppm. The granule cell layer of animals exposed to 100 ppm appeared qualitatively normal. The alterations reported here support the few earlier reports of morphological alterations in the CNS of adult laboratory animals. Effects of **toluene** similar to those described, that is alterations in specific neuron populations and their afferent and efferent terminal fields may complement changes in neurophysiology and behavior that have been observed in prenatally and perinatally exposed rodent pups. Causal relationships, however, remain to be elucidated.
[Slomianka L et al; Toxicol 62 (2): 189-202 (1990)]**PEER REVIEWED**

The aim of the present study was to investigate the effects of **toluene** on fetal development in well nourished and malnourished rats. Long-term behavioral consequences after in utero exposure were also studied. **Toluene** (1.2 g/kg sc) was administered daily to well nourished and to malnourished (food restricted to 50% of ad libitum intake) pregnant rats, during the second (8-15 days) or the third week of pregnancy (14-20 days). Offspring were evaluated for malformation, development of the skeleton, prenatal growth of the brain and liver, postnatal growth and long lasting behavioral effects. In utero exposure to **toluene** during the third week of pregnancy resulted in low body weight at birth, which persisted in the male offspring into adulthood. Malnutrition increased fetal susceptibility to the effects of **toluene** as indicated by evaluation of the development of the skeleton. Behavioral tests performed when the pups were 30 and 90 days old showed effects of in utero malnutrition (increased ambulation and worse performance in a shuttle box), but no behavioral effects related to **toluene** exposure were detected. These data indicate that in utero exposure to **toluene** can have long lasting effects on body growth and that maternal malnutrition increases the risk for **toluene** fetotoxicity.
[Silva V AD et al; Toxicol 64 (2): 155-68 (1990)]**PEER REVIEWED**

Toluene did not induce gene mutations in Salmonella typhimiurium strain TA98, TA100, TA1535, or TA1537 with or without exogenous metabolic activation. In the mouse lymphoma assay, **toluene** gave an equivocal response with and without exogenous metabolic activation. **Toluene** did not induce sister chromatid exchanges or chromosomal aberrations in Chinese hamster ovary cells in the presence or absence of exogenous metabolic activation.

[DHHS/NTP; Toxicology and Carcinogenesis Studies of Chlorobenzene in F344/N Rats and B6C3F1 Mice (Inihalation Studies) p.4 (1990) Technical Rpt Series No. 371 NIH Pub No. 90-2826]**PEER REVIEWED**

... **Toluene** can alter learned behavior at concentrations below anesthetic levels but, in general, above 1000 ppm.
[Klaassen, C.D., M.O. Amdur, Doull J. (eds.). Casarett and Doull's Toxicology. The Basic Science of Poisons. 5th ed. New York, NY: McGraw-Hill, 1995. 747]**PEER REVIEWED**

Toluene was injected into the yolk sac of fresh fertile chicken eggs prior to incubation. Hatchability of the eggs was 85%, 25%, and 0 with exposures of 4.3, 8.7, and 17.4 mg/egg, respectively.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47 96 (1989)]**PEER REVIEWED**

Toluene was reported to induce chromosomal aberrations in the bone marrow cells of male albino rats after chronic inhalation exposure to 5.4 or 50.7 mg/cu m on 4 hr/day, five days/wk for four months or after sc injection of 0.8 g/kg bw. Chromosomal aberrations in bone marrow cells were reported following sc injection of 1 g/kg bw daily for 12 days to male albino rats.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47 98 (1989)]**PEER REVIEWED**

Toluene and benzene administered concurrently were reported to have an additive effect on induction of chromosomal aberrations. **Toluene** reduced the number of sister chromatid exchanges induced by benzene when both compounds were administered intraperitoneally to DBA/2 mice and reduced the clastogenic activity of benzene when the two compounds were simultaneously administered orally to CD-1 mice, intraperitoneally to Sprague-Dawley rats, or subcutaneously to NMRI mice.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47 99 (1989)]**PEER REVIEWED**

Animal studies in mice exposed to **toluene** at concentrations of 2.5-500 ppm demonstrated decreased host defense to respiratory infections.
[Sullivan, J.B. Jr., G.R. Krieger (eds.). Hazardous Materials Toxicology-Clinical Principles of Environmental Health. Baltimore, MD: Williams and Wilkins, 1992. 1092]**PEER REVIEWED**

The cardiovascular response of 25 mongrel dogs following exposure to 30,000 ppm **toluene** for 9-10 min was complex. For most of the animals, there was no change in electrocardiogram readings for the first 3-4 min of exposure. The heartbeat then became rapid for several minutes, and was followed by a period of bradycardia. Immediately before death ventricular fibrillation was noted. ... Four of the dogs were particularly sensitive, their ventricular arrhythmias were transient and accompanied by fluctuations of blood pressure. The authors suggested that **toluene** had a direct effect on the septal and ventricular

muscles of the heart which permitted the development of fatal arrhythmias in sensitive dogs.
[Ikeda N et al; Forensic Sci Intern 44: 151-8 (1990) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.31 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

Mice exposed for 3 hr to **toluene** at concentrations of 2.5-500 ppm exhibited increased, but not dose-related, susceptibility to respiratory infections when challenged by Streptococcus zooepidemicus. Pulmonary bactericidal activity was decreased at concentrations of 2.5 ppm and 100-500 ppm but not at concentrations of 5-50 ppm. There was no effect on susceptibility to infection with a **toluene** exposure of 1 ppm for 3 hr, 5 days (3 hr/day) or 4 wk (3 hr/day). The bactericidal activity of the lung was decreased during the 5-day treatment but not with the 4-wk treatment. The authors hypothesized that **toluene** exerted an adverse effect on alveolar macrophage function, thereby decreasing disease resistance.
[Aranyi C et al; Toxicol Lett 25: 103-10 (1985) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.39 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

Studies have demonstrated that **toluene** can produce subtle changes in the auditory system. Intermediate exposure to **toluene** produced a permanent loss of hearing in the high frequency range (approximately 16 kHz) in rats exposed to 1200 ppm for 5-9 wk or 1000 ppm for 2 wk.
[Pryor GT, Rebert CS; Neurotoxicology 13: 225-34 (1992) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.44 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

In 3-day-old rats, daily 15 min exposures to **toluene** resulted in a dose-related increase in righting-reflex latency time. At each dose the righting-reflex latency decreased over the first 4 wk of exposure indicating that the animals had developed at least partial tolerance to the **toluene**. During the second 4-wk period, latencies increased again at the higher doses but were never as great as they were for the initial **toluene** exposure. The results for the second 4-wk period showed that there were limitations to the adaptive response at the higher **toluene** doses and that there were cumulative effects of exposure at these doses. Tolerance was probably the result of induction of **toluene** metabolizing enzymes.
[Lorenzana-Jimenez M, Salas M; Neurotoxicol Teratol 12: 353-7 (1990) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.45 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

Concentrations of 480 ppm and above decreased the ability of trained rats to perform a sequence of lever press actions associated with a reward (milk). During training, the rats were divided into two groups. The reward presentation for one group was not accompanied by any noticeable external events. For the second group, the reward presentation was accompanied by light and sound stimuli. The effects of **toluene** on performance were less severe with the rats trained using the light and sound reinforcement. This suggests that behavior associated with external signals is less subject to disruption by **toluene** than behavior that is not accompanied by external reinforcement.
[Wood RW et al; Toxicol Appl Pharmacol 68: 462-72 (1983) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances &

Disease Registry; Toxicological Profile for Toluene (Update) p.45 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

Age ... influences neurological response after exposure to **toluene**. Young rats (50 days old) were affected by **toluene** to a lesser extent than older rats (120 days old) based on several measurements of escape latency 30 days after exposure to 30,000-40,000 ppm for 15 min/day.
[Castilla-Serna L et al; Arch Invest Med 22: 295-301 (1991) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.46 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

Toluene exposure ... changes sleep patterns in animals. Both single episodes of **toluene** exposure (about 1000 ppm) and subchronic 8 hr/day exposures for 3 wk (about 600 ppm), changed patterns of sleep and wakefulness in rats. After the single exposures, there was a decrease in wakefulness and an increase in slow-wave sleep; a prolonged sleep latency was apparent for the 2 days following exposure. Latency was defined as the time interval between the end of the exposure period and the beginning of a particular phase of the sleep cycle. Following the 3 wk exposures, there was an increase in wakefulness during the dark period on the 2 days after exposure and a decrease in slow wave sleep on the first day.
[Arito H et al; Arch Toxicol 62: 76-80 (1988) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.46 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

Brain levels of norepinephrine, dopamine, serotonin, vanillylmandelic acid, homovanillic acid, and 5-hydroxyindolacetic acid were altered in six areas of the brain in male CD-1 mice administered **toluene** (5-105 mg/kg/day) in their drinking water for a 28-day period. Significant increases of norepinephrine, dopamine, and serotonin were present in the hypothalamus at all dose levels. The maximum increase occurred with the 22 mg/kg/day dose and there were lesser increases for both the 5 and 105 mg/kg/day doses, giving biphasic response. Roughly similar fluctuations were seen in the concentrations of vanillylmandelic acid and homovanillic acid, which are metabolites of dopamine and norepinephrine and 5-hydroxyindolacetic acid, a serotonin metabolite. In corpus striatum, the levels of dopamine and serotonin were significantly increased at the two highest doses. The level of vanillylmandelic acid was also increased significantly at the same doses. In the medulla oblongata, the concentrations of norepinephrine, vanillylmandelic acid, and 5-hydroxyindolacetic acid were significantly increased at the 22 mg/kg/day dose, but not at the other doses, while the levels of serotonin were significantly increased at the 22 and 105 mg/kg/day doses. Norepinephrine concentrations were elevated in the midbrain. ...
[U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.61 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

To identify the frequency range most sensitive to **toluene**-induced auditory damage, the auditory function of adult Long-Evans rats exposed to 1750 ppm of **toluene** (6 h/day, 5 days/week, 4 weeks), was tested by recording auditory-evoked potentials directly from the round window of the cochlea. The present electrocochleographic findings do not support a specific mid- to high-frequency loss of auditory sensitivity. On the contrary, the electrophysiologic data, obtained for audiometric frequencies ranging from 2 to 32 kHz, showed a hearing deficit not only in the mid-frequency region (12-16 kHz), but also in the mid-low-frequency region (3-4 kHz). Actually, the effect of **toluene** was independent of the

frequency in our experimental conditions. Histological analysis was consistent with electrophysiologic data because a broad loss of outer hair cells occurred in both mid- and mid-apical coil of the organ of Corti.
[Lataye R et al; Neurotoxicol Teratol 21 (3): 267-76 (1999)]**PEER REVIEWED**

National Toxicology Program Studies:

Long-term studies were conducted by exposing groups of 60 rats /F344/N/ of each sex to 0, 600, or 1,200 ppm **toluene** by inhalation, 6.5 hours per day, 5 days per week. Groups of 60 /B6C3F1/ mice of each sex were exposed at 0, 120, 600, or 1,200 ppm on the same schedule. ... Animals were exposed to **toluene** for 103 weeks. Nephropathy was seen in almost all rats, and the severity was somewhat increased in exposed rats. A rare renal tubular cell carcinoma in a female rat and an equally uncommon sarcoma of the kidney in another female rat were seen in the 1,200 ppm exposure group. Erosion of the olfactory epithelium and degeneration of the respiratory epithelium were increased in exposed rats. Inflammation of the nasal mucosa and metaplasia of the olfactory epithelium were increased in exposed female rats. A rare squamous cell carcinoma of the nasal mucosa was seen in one female rat at 1,200 ppm. A squamous cell papilloma of the forestomach was observed in one female rat at 1,200 ppm, and a squamous cell carcinoma was observed in a second female rat at 1,200 ppm. No chemically related neoplasms were found in male rats, and the one nasal, two kidney, and two forestomach neoplasms observed in female rats were considered not to be associated with inhalation exposure to **toluene**. For mice, no biological important increases were observed for any nonneoplastic or neoplastic lesions.
[DHHS/NTP; Toxicology and Carcinogenesis Studies of Chlorobenzene in F344/N Rats and B6C3F1 Mice (Inhalation Studies) p.4 (1990) Technical Rpt Series No. 371 NIH Pub No. 90-2826]**PEER REVIEWED**

Non-Human Toxicity Values:

LD50 Rat oral 2.6 to 7.5 g/kg
[DHHS/NTP; Toxicology and Carcinogenesis Studies of Chlorobenzene in F344/N Rats and B6C3F1 Mice (Gavage Studies) p.16 (1990) Technical Rpt Series No. 371 NIH Pub No. 90-2826]**PEER REVIEWED**

LD50 Rabbit dermal 14.1 ml/kg
[DHHS/NTP; Toxicology and Carcinogenesis Studies of Chlorobenzene in F344/N Rats and B6C3F1 Mice (Gavage Studies) p.16 (1990) Technical Rpt Series No. 371 NIH Pub No. 90-2826]**PEER REVIEWED**

LD50 Rat (female) ip 1.64 g/kg
[DHHS/NTP; Toxicology and Carcinogenesis Studies of Chlorobenzene in F344/N Rats and B6C3F1Mice (Inhalation Studies) p.16 (1990) Technical Rpt Series No. 371 NIH Pub No. 90-2826]**PEER REVIEWED**

LD50 MOUSE IP 1.15 G/KG
[KOGA K, OHMIYA Y; J TOXICOL SCI 3 (1): 25 (1978)]**PEER REVIEWED**

LD50 Rat oral 5000 mg/kg
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996.

3190]**PEER REVIEWED**

LD50 Rat ip 1332 mg/kg
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 3190]**PEER REVIEWED**

LD50 Rat iv 1960 mg/kg
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 3190]**PEER REVIEWED**

LC50 Mouse ihl 400 ppm/24 hr
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 3190]**PEER REVIEWED**

LD50 Mouse ip 59 mg/kg
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 3190]**PEER REVIEWED**

LD50 Mouse sc 2250 mg/kg
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 3190]**PEER REVIEWED**

LD50 Mouse ip 640 mg/kg
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 3190]**PEER REVIEWED**

LD50 Rabbit skin 12,124 mg/kg
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 3190]**PEER REVIEWED**

... The LC50 for **toluene** in mice is 5320 ppm/8 hr /via inhalation/ ...
[Klaassen, C.D., M.O. Amdur, Doull J. (eds.). Casarett and Doull's Toxicology. The Basic Science of Poisons. 5th ed. New York, NY: McGraw-Hill, 1995. 746]**PEER REVIEWED**

As the duration of **toluene** inhalation exposure increased, the LC50 in rats decreased from 26,700 ppm for 1 hr, to 12,200 ppm for 2-2.5 hr, to 8000 ppm for 4 hr.
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Volumes I,II, III. Cincinnati, OH: ACGIH, 1991. 1568]**PEER REVIEWED**

Ecotoxicity Values:

LC50 FOR BLUEGILL WAS 17 MG/L/24 HR & 13 MG/L/96 HR (95% CONFIDENCE LIMIT 11-15 MG/L) @ 21-23 DEG C AFTER EXPOSURE TO **TOLUENE**. /CONDITIONS OF BIOASSAY NOT SPECIFIED/
[BUCCAFUSCO RJ ET AL; BULL ENVIRONM CONTAM TOXICOL 26 (4): 446-52 (1981)]**PEER REVIEWED**

LC50 Palaemonetes pugio (grass shrimp) 9.5 mg/l/96 hr /Conditions of bioassay not specified/
[Verschueren, K. Handbook of Environmental Data on Organic Chemicals. 3rd ed. New York, NY: Van Nostrand Reinhold Co., 1996. 1727]**PEER REVIEWED**

LC50 Cancer magister (crab larvae stage I) 28 mg/l/96 hr /Conditions of bioassay not specified/
[Verschueren, K. Handbook of Environmental Data on Organic Chemicals. 3rd ed. New York, NY: Van Nostrand Reinhold Co., 1996. 1727]**PEER REVIEWED**

LC50 Crangon franciscorum (shrimp) 4.3 mg/l/96 hr /Conditions of bioassay not specified/
[Verschueren, K. Handbook of Environmental Data on Organic Chemicals. 3rd ed. New York, NY: Van Nostrand Reinhold Co., 1996. 1728]**PEER REVIEWED**

LC50 Pimephales promelas (fathead minnow) 56-34 mg/l/24-96 hr /Conditions of bioassay not specified/
[Verschueren, K. Handbook of Environmental Data on Organic Chemicals. 3rd ed. New York, NY: Van Nostrand Reinhold Co., 1996. 1728]**PEER REVIEWED**

LC50 Lebistes reticulatus (guppy) 63-59 mg/l/24-96 hr /Conditions of bioassay not specified/
[Verschueren, K. Handbook of Environmental Data on Organic Chemicals. 3rd ed. New York, NY: Van Nostrand Reinhold Co., 1996. 1729]**PEER REVIEWED**

LC50 Channel catfish 240 mg/l 96 hr /Conditions of bioassay not specified/
[Environment Canada; Tech Info for Problem Spills: Toluene p.71-75 (1981)]**PEER REVIEWED**

LC50 Pimephales promelas (fathead minnow) 34.27 mg/l 96 hr (95% Confidence Limits= 22.83-45.86 mg/l) /Conditions of bioassay not specified/
[Pickering QH, Henderson C; J Water Pollution Control Fed 38: 1419-1429 (1966) as cited in NRC; Alkyl Benzenes p.352 (1981)]**PEER REVIEWED**

LC50 Carassius auratus (goldfish) 57.68 mg/l 96 hr (95% Confidence Limits= 48.87-68.75 mg/l) /Conditions of bioassay not specified/
[Pickering QH, Henderson C; J Water Pollution Control Fed 38: 1419-1429 (1966) as cited in NRC; Alkyl Benzenes p.352 (1981)]**PEER REVIEWED**

LC50 Lebistes reticulatus (guppy) 59.30 mg/l 96 hr (95% Confidence Limits= 50.87-70.34 mg/l) /Conditions of bioassay not specified/
[Pickering QH, Henderson C; J Water Pollution Control Fed 38: 1419-1429 (1966) as cited in NRC; Alkyl Benzenes p.352 (1981)]**PEER REVIEWED**

LC50 Daphnia magna, (water flea) 313 mg/l 48 hr /Conditions of bioassay not specified/
[USEPA. In Depth Studies on Health and Environ Impact of Sel Water Poll (1978) EPA 68-01-4646 as cited in NRC; Alkyl Benzenes p.356 (1981)]**PEER REVIEWED**

LC50 Nitocra spinipes (copepod) 24.2-74.2 mg/l 24 hr /Conditions of bioassay not specified/
[Potera GT; Effects of Benzene, Toluene, and Ethylbenzene on Several Important Members of the Estuarine Ecosystem Ph.D. Dissertation p.1-117 (1975) as cited in NRC; Alkyl Benzenes p.355 (1981)]**PEER REVIEWED**

LC50 Artemia salina (brine shrimp) 33 mg/l 24 hr /Conditions of bioassay not specified/
[Price KS et al; J Water Pollut Control Fed 46: 63-77 (1974) as cited in NRC; Alkyl Benzenes p.355 (1981)]**PEER REVIEWED**

LC50 Morone saxatilis (striped bass) 7.3 mg/l 96 hr /Conditions of bioassay not specified/
[Benville PE, Korn S; Calif Fish Game 63: 204-209 (1977) as cited in NRC; Alkyl Benzenes p.353 (1981)]**PEER REVIEWED**

LC50 Cyprinodon variegatus (sheepshead minnow) 277-485 mg/l 96 hr /Conditions of bioassay not specified/
[NRC; Alkyl Benzenes p.354 (1981)]**PEER REVIEWED**

LC50 Aedes aegypti-4th instar (mosquito larvae) 22 mg/l /Conditions of bioassay not specified/
[USEPA. In Depth Studies on Health Environ Impact of Sel Water Pollutants (1978) EPA 68-01-4646 as cited in NRC; Alkyl Benzenes p.362 (1981)]**PEER REVIEWED**

LC50 Calandra granaria (grain weevil) 210 mg/l /in air/
[Ferguson J, Pirie H; Ann Appl Biol 35:532-550 (1948) as cited in NRC; Alkyl Benzenes p 362 (1981)]**PEER REVIEWED**

LC50 Pimephales promelas (fathead minnows) 55-72 mg/l (embryos), 25-36 mg/l (1-day posthatch protolarvae), and 26-31 mg/l (30-day-old minnows)/ 96 hour /Conditions of bioassay not specified/
[Devlin EW et al; Bull Environ Contam Toxicol 29 (1): 12-17 (1982)]**PEER REVIEWED**

EC50 Pimephales promelas (fathead minnow) 14.6 mg/l/96 hr (confidence limit 14.0 to 15.1 mg/l), flow-through bioassay with measured concentrations, 24.7 deg C, dissolved oxygen 6.9 mg/l, hardness 45.4 mg/l calcium carbonate, alkalinity 43.4 mg/l calcium carbonate, and pH 7.89. Effect: loss of equilibrium.
[Geiger D.L., Poirier S.H., Brooke L.T., Call D.J., eds. Acute Toxicities of Organic Chemicals to Fathead Minnows (Pimephales

Promelas). Vol. III. Superior,Wisconsin: University of Wisconsin-Superior, 1986. 163]**PEER REVIEWED**

LC50 Pimephales promelas (fathead minnow) 36.2 mg/l/96 hr (confidence limit 29.4 to 44.6 mg/l), flow-through bioassay with measured concentrations, 24.7 deg C, dissolved oxygen 6.9 mg/l, hardness 45.4 mg/l calcium carbonate, alkalinity 43.4 mg/l calcium carbonate, and pH 7.89.
[Geiger D.L., Poirier S.H., Brooke L.T., Call D.J., eds. Acute Toxicities of Organic Chemicals to Fathead Minnows (Pimephales Promelas). Vol. III. Superior,Wisconsin: University of Wisconsin-Superior, 1986. 163]**PEER REVIEWED**

TSCA Test Submissions:

Neurotoxicity was determined in groups of rats (4 male and 4 female, strain not reported) exposed by inhalation to 0,100, or 1500 ppm **toluene** (purity not reported) 6 hrs/day, 5 days/week for periods up to 27 weeks. Histological sections of selected areas of the brainstem were made for the upper medulla oblongata (including dorsal and ventral cochlear and vestibular nuclei), lower metencephalon (including superior olivary nuclei, trapezoid body and ventral cochlear nuclei), upper metencephalon (including the lateral lemniscus, superior olivary nuclei, cochlear and vestibular nuclei, and inferior colliculus) and the mesencephalon-diencephalon junction (including the medial geniculate). The investigators reported that the "vast majority" of sections from animals exposed to **toluene** were indistinguishable from controls. Shrunken and darkly stained neurons were observed in the corpus trapezoid of one animal exposed to 100 ppm and another exposed to 1500 ppm **toluene**; these were present in only one section and not in sufficient quantity to be considered a positive response by the investigators. Statistical analysis of the results was not reported.
[American Petroleum Inst.; Effects of Toluene Exposure on Auditory Pathways, Final Report. (1979), EPA Document No. 40-8450019, Fiche No. OTS0507495] **UNREVIEWED**

Chronic toxicity was evaluated in male and female Sprague Dawley rats (15/sex/group) exposed to **toluene** via inhalation at 0, 100 and 1500 ppm for 6 hrs/day, 5 days/week for 26 weeks. There were significant increases in the hematocrit and hemoglobin levels in females at 1500 ppm in the 13th week. There were significant differences in females at week 26 in the following: decreased mean blood clotting time and increased mean serum glutamic pyruvic transaminase at 100 ppm level, and decreases in glucose levels at 1500 ppm. There were no significant differences between treated and control animals in urinalysis.
[American Petroleum Institute; 26 Week Inhalation Toxicity Study in the Rat (1980), EPA Document No. FYI-AX-1081-0136, Fiche No. 0136-0] **UNREVIEWED**

Teratogenicity was evaluated in mated female CRL:COBS CD (SD) BR rats (27/group) exposed to **toluene** by inhalation at nominal concentrations of 0, 100 or 400 ppm on gestation days (GD) 6-15 for 6 hrs/day. The adult female rats were sacrificed on GD 20 and examined. There were no significant differences observed between treated and control animals in the following: maternal mortality, body weights, food consumption, examination of tissues and organs at necropsy (except an insignificant number of observations of mottled lungs in 4 high-dose group rats), pregnancy rate, live litters, implantation sites, resorptions, litters with resorptions, dead pups, litters with dead pups, live

pups/implantation site, mean live litter size, average pup weights, fetal sex ratio, examination of soft tissues of the head, thoracic and visceral organs, and skeletal abnormalities.
[Litton Bionetics, Inc.; Teratology Study in Rats, Toluene, Final Report (1978), EPA Document No. 87-8210353, Fiche No. OTS0205936] **UNREVIEWED**

The ability of **toluene** to induce specific locus mutations at the TK locus in cultured L5178Y mouse lymphoma cells (Mouse Lymphoma Mutagenesis Assay) was evaluated in the presence and absence of mouse liver S9 metabolic activation. Based on preliminary toxicity tests, both nonactivated and S9-activated cultures were treated with 0.30, 0.20, 0.15, 0.10, or 0.050 ul/ml produced a range of 7 - 78% total growth for nonactivated cultures and from 60 - 138% total growth for S9-activated cultures. None of the nonactivated or activated cultures produced mutant frequencies significantly greater than the solvent (DMSO) controls.
[Litton Bionetics, Inc.; Mutagenicity Evaluation of Toluene. (1978), EPA Document No. 878210352, Fiche No. OTS0205936] **UNREVIEWED**

The mutagenicity of **toluene** was evaluated in Salmonella tester strains TA98, TA100, TA1535, TA1537 and TA1538, and the yeast Saccharomyces cerevisiae tester strain D4, both in the presence and absence of added metabolic activation by Aroclor-induced rat liver S9 fraction. Based on preliminary bacterial toxicity determinations, **toluene**, diluted with acetone, was tested for mutagenicity at concentrations up to 5.0 ul/plate using both the plate and suspension assay methods. **Toluene** did not cause a positive response in any of the bacterial or yeast tester strains, either with or without metabolic activation.
[Litton Bionetics, Inc.; Mutagenicity Evaluation of Toluene. (1978), EPA Document No. 878210352, Fiche No. OTS0205936] **UNREVIEWED**

The mutagenicity of **toluene** was evaluated in a dominant lethal assay using three groups of male CD-1 mice (12/group) receiving whole body exposures to nominal concentrations of test material at 0, 100 or 400 ppm for 6 hrs/day, 5 days/week for 8 weeks. Following exposure, each male was mated with two untreated females/week for two consecutive weeks. Females were sacrificed 14 days after the midweek of mating. There was no effect of treatment for all dosed male mice as indicated by mortality, body weight and in-life physical observations. There were no significant differences between treated and control females with respect to fertility indices, average number of implants/pregnant female, average number of dead implants/pregnant female, and proportions of female with one or more dead implants.
[Litton Bionetics, Inc.; Mutagenicity Evaluation of Toluene, Mouse Dominant Lethal Assay, Final Report. (1981), EPA Document No. FYI-AX-1081-0136, Fiche No. OTS0000136-0] **UNREVIEWED**

The ability of **toluene** to cause chromosome aberrations in the bone marrow cells of male Charles River rats exposed by intraperitoneal injection at dose levels of 0, 0.025, 0.082 or 0.247 cc/kg (in DMSO solvent, 0.65 cc/rat/day), either once in an acute study (15 rats/group) or once each day for 5 days in a subchronic study (5 rats/group) was evaluated. Five rats/group in the acute study were sacrificed 6, 24 or 48 hrs following dosing and the rats in the subchronic study were sacrificed 6 hrs after administration of the last dose. 50 cells/animal were scored for chromosome aberrations. None of the cells from any of the treated animals exhibited a significant increase in the frequency of chromosome aberrations.
[Litton Bionetics, Inc.; Mutagenicity Evaluation of Toluene. (1978), EPA Document No. 878210352, Fiche No. OTS0205936] **UNREVIEWED**

The percutaneous absorption of **toluene** was evaluated in six human volunteers. A glass ring having an area of 13cm(2) was placed against the palm and 2ml of 14C-**toluene** was applied. After one minute the ring was removed and adherent liquid allowed to evaporate. All urine was collected and analyzed for radioactive content until background levels of activity were approached. **Toluene** absorption was very low, averaging .022ul/cm(2) for the six human subjects.
[Thomas J. Franz M.D.; Absorption of Petroleum Products Across the Skin of Man and Monkey, Draft Report, (no date), EPA Document No. FYI-AX-0187-0185, Fiche No. OTS0000185-4] **UNREVIEWED**

Metabolism/Pharmacokinetics:

Metabolism/Metabolites:

Toluene is extensively metabolized via oxidation to benzyl alcohol then to benzaldehyde by alcohol dehydrogenase. Further oxidation then forms benzoic acid. Conjugation with glycine produces the major metabolite, hippuric acid, which is excreted in the urine. Benzyl glucuronide is formed in smaller amounts by conjugation with glucuronic acid.
[Haddad, L.M., Clinical Management of Poisoning and Drug Overdose. 2nd ed. Philadelphia, PA: W.B. Saunders Co., 1990. 1224]**PEER REVIEWED**

IN PRINTERS EXPOSED TO AIR CONTAINING **TOLUENE** (AVG CONCN 23 PPM), URINARY EXCRETION OF O-CRESOL, WHICH IS NOT A NORMAL CONSTITUENT OF URINE, WAS OBSERVED. APPARENTLY, **TOLUENE** WAS OXIDIZED AT AROMATIC NUCLEUS FORMING CRESOLS, BESIDES HIPPURIC ACID.
[ANGERER J; INT ARCH OCCUP ENVIRON HEALTH 43 (1): 63 (1979)]**PEER REVIEWED**

In rats, approx 0.5%-1.1% of the dose is converted to o-cresol and p-cresol and is excreted as glucuronide and sulfate conjugates.
[Bakke OM, Scheline RR; Tox Appl Pharm 16: 691-700 (1970) as cited in NRC; Alkyl Benzenes p.221 (1981)]**PEER REVIEWED**

In mammalian species, acidic metabolites are conjugated with glycine to form hippuric acid and phenylacetic acid. In humans, the phenylacetic acid metabolite is also conjugated with glutamine to form phenacetylglutamine.
[James MO et al; Proc R Soc Lond Ser B 182: 25-35 (1972) as cited in NRC; Alkyl Benzenes p.219 (1981)]**PEER REVIEWED**

The association between occupational **toluene** exposure and blood and adipose tissue **toluene** concentrations was examined. Breathing zone samples were monitored for **toluene** in two Swedish rotogravure printing facilities. Sc adipose tissues were taken from 37 workers after work on Thursday or Friday and analyzed for **toluene**. Venous blood samples were taken from 11 workers after work on Friday and at various times over the following weekend and assayed for **toluene**. Blood and adipose tissue samples were obtained from 11 other workers immediately after work and after 63 and 135 hours nonexposure and analyzed for **toluene**. Blood samples were also taken from 21 unexposed workers and analyzed for **toluene**. Attempts were made to fit the blood **toluene** data to various pharmacokinetics models. Airborne **toluene** concentrations in the printing factories ranged from 8 to 416 mg/cu m, median 75 mg/cu m. Blood **toluene** concentrations in the unexposed workers were below the detection limit,

0.01 umole/l. Blood samples obtained immediately after work contained 0.22 to 21.4 umole/l **toluene**. Elimination of **toluene** from the blood could be described by a three compartment model having median halftimes of 9 minutes, 2 hours, and 79 hours. **Toluene** was eliminated from adipose tissue with a median halftime of 79 hours. Adipose tissue concentrations were significantly associated with the workers' exposure to airborne **toluene** during the previous week. Adipose tissue **toluene** concentrations were significantly correlated with blood **toluene** concentrations after 70 hours exposure. It was concluded that the prolonged presence of **toluene** in the blood means that there is an endogenous exposure from adipose tissue depots that continues long after occupational exposure has ended.
[Nise G et al; Br J Ind Med 46 (6): 407-11 (1989)]**PEER REVIEWED**

Evidence has suggested that there is an ethnic related difference in organic solvent metabolism in humans; analyses were thus made to obtain evidence of strain differences in animals to assist in consolidating the observation in workers. Female Donryu, Fischer, Sprague-Dawley, and Wistar rats were exposed to **toluene** at dose levels of 5, 45, 500, 2500, and 3500 ppm for 8 hours in a dynamic flow type exposure system. Urine samples were collected for 24 hours from the start of exposure. While the variation in free p-cresol excretion was wide among the rats of the same strain exposed to **toluene** at the same concentration, it was also noted that the four strains tested could be classified into two groups depending on the free p-cresol levels at **toluene** concentrations up to 500 ppm. No significant differences were noted between Sprague-Dawley and Wistar strains nor between Donryu and Fischer strains at the 45 and 500 ppm levels. However, there were significant differences between these two groups. At higher concentrations of 2500 and 3500 ppm, the increase in the free p-cresol levels was remarkable only in Donryu rats, reaching the levels of Sprague-Dawley and Wistar rats, while the level in Fischer rats remained unchanged.
[Inoue O et al; Bull Environ Contam Toxicol 43 (1): 74-9 (1989)]**PEER REVIEWED**

The mutual metabolic suppression between benzene and **toluene** was studied. The subjects, 190 male Chinese workers employed in shoe manufacturing, printing, audio equipment manufacture, and automobile industries, were divided into four groups based on occupational exposure: 65 were exposed to benzene, 35 to **toluene**, 55 to both compounds, and 35 served as comparisons. The arithmetic mean exposure level of benzene was 31.9 and of **toluene** 44.7 ppm. The mixture contained benzene at 17.9 +/29.3 and **toluene** at 20.5 +/25.8 ppm. The exposure levels were measured using individuals diffusive samplers. The geometric mean levels of the metabolites, phenol, catechol, hydroquinone, hippuric acid, and o-cresol, in unexposed workers were 6.9, 9.4, 4.8, 72.5, and 0.066 mg per liter, respectively. Values corrected for creatinine and specific gravity were different from the values cited above. Multiple correlation coefficients for benzene exposure versus its three metabolites were for phenol, 0.740; for catechol, 0.629; and for hydroquinone, 0.726. Multiple correlation coefficients for **toluene** and its two metabolites were 0.649 for hippuric acid and 0.583 for o-cresol. The slopes of regression lines for the exposure to benzene in the presence of **toluene** were less than half of those obtained when the workers were exposed to benzene alone; however, the regression lines for benzene in mixture versus catechol were about 80% or higher than the lines observed with benzene as the sole pollutant. The regression lines for **toluene** in the mixture and excretion level of hippuric acid and o-cresol showed reduced metabolic conversion compared to when exposure was limited to **toluene** alone. It was concluded that simultaneous exposure to benzene and **toluene** results in mutual suppression of metabolism yielding the urinary metabolites phenol, hydroquinone, hippuric acid, and o-cresol.
[Inoue O et al; Int Arch Occup Environ Health 60 (1): 15-20

(1988)]**PEER REVIEWED**

Absorption, Distribution & Excretion:

TOLUENE VAPOR IS READILY ABSORBED BY INHALATION AND THE LIQUID BY THE GI TRACT, BUT POORLY FROM THE SKIN.
[Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965. 68]**PEER REVIEWED**

IN DOGS SUBJECTED TO INHALATION ... HIGHEST CONCENTRATIONS WERE FOUND IN THE ADRENALS (20 UG/G), BRAIN (19 UG/G IN CEREBELLUM & 18 UG/G IN CEREBRUM), AND BONE MARROW (18 UG/G).
[Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965. 69]**PEER REVIEWED**

ALTHOUGH SOME ABSORBED **TOLUENE** MAY BE REEXHALED BY LUNG, MAJOR EXCRETORY PATHWAY IS RAPID OXIDATION OF **TOLUENE** TO BENZOIC ACID, WHICH IS CONJUGATED WITH GLYCINE & EXCRETED AS HIPPURIC ACID IN URINE. ... WITHIN REASONABLE LIMITS, EXCRETION OF HIPPURIC ACID IN URINE IS PROPORTIONAL TO EXPOSURE. AN EXPOSURE OF 200 PPM OF **TOLUENE** RESULTED IN EXCRETION OF 3.5 G HIPPURIC ACID PER LITER OF URINE (SPECIFIC GRAVITY 1.016).
[Doull, J., C.D. Klaassen, and M. D. Amdur (eds.). Casarett and Doull's Toxicology. 2nd ed. New York: Macmillan Publishing Co., 1980. 489]**PEER REVIEWED**

SIX SUBJECTS EXPOSED TO **TOLUENE** IN INSPIRED AIR (50, 100, 150 PPM) SHOWED LITTLE DIFFERENCE IN RATE OF RESP SOLVENT UPTAKE. NO SIMPLE RELATION EXISTED BETWEEN UPTAKE RATE & PERIPHERAL VENOUS CONCN, INDICATING THAT NO CALCULATION COULD BE MADE FOR TOXIC DOSE OF INNER ORGANS. DIFFERENCES IN RESP EXCRETION WAS EXPLAINED BY RESP MINUTE VOL IN POST-EXPOSURE PERIOD, &, AFTER EXPOSURE AT REST, THE AMT OF BODY FAT.
[VEULEMAN H ET AL; INT ARCH OCCUP ENVIRON HEALTH 42 (2): 105 (1978)]**PEER REVIEWED**

FOLLOWING SINGLE IP ADMIN OF (14)C-LABELED **TOLUENE** (290 UG/KG) TO MICE, HIGHEST LEVEL OF RADIOACTIVITY WAS FOUND IN ADIPOSE TISSUE, FOLLOWED IN DESCENDING ORDER BY KIDNEY, LIVER & LUNG. LOWEST ACTIVITY WAS IN BRAIN TISSUE & BLOOD/BRAIN RATIO WAS ABOUT 0.4.
[KOGA K; FOLIA PHARMACOL JPN 74 (6): 687 (1978)]**PEER REVIEWED**

The blood/gas partition coefficient ranges from 12.4 to 15.6.
[NRC; Alkyl Benzenes p.220 (1981)]**PEER REVIEWED**

At equilibrium, the avg **toluene** concn per liter of blood is 2.4 mg for each 100 ppm **toluene** in the envir air.
[Cleland, J.G., G.L. Kingsbury. Multimedia Environmental Goals for Environmental Assessment. Volume 1. EPA-600/7-77-136a. Research Triangle Park, NC: EPA, Nov. 1977.,p. E-146]**PEER REVIEWED**

... Whole body autoradiography has been modified and applied to distribution studies of ... **toluene**. ... [Bergman K; CRC Crit Review Toxicol 12 (1): 59-118 (1983)]**PEER REVIEWED**

The urinary excretion of hippuric acid and o-cresol in humans was measured after a 7 hr exposure to **toluene** at a constant concn of 100 ppm but with a time-weighted avg of 100 ppm. In study A, 4 men were exposed to clean air and to constant and varying concns of **toluene** in combination with rest and with 100 W exercise for 140 min exercise increased the end-exposure excretion rate of hippuric acid and o-cresol by 47 and 114%, respectively. After exposure, all excess hippuric acid was excreted within 4 hr, while o-cresol was eliminated with a half-life of approx 3 hr. Alveolar air concn of **toluene** was 21-31 ppm during constant exposure and 13-57 ppm during varying exposure, but no difference in mean alveolar **toluene** concn or in metabolite excretion was seen between the exposure schedules. In study B, 32 men and 39 women aged between 31 and 50 yr were exposed once to either clean air or ... or varying concns of **toluene**. The background excretion rate of hippuric acid was 0.97 mg/min (1.25 g/g creatinine) and rose to 3.74 mg/min (3.90 g/g creatinine) during the last 3 hr of exposure to 100 pmm **toluene**. The corresponding figures for o-cresol were 0.05 ug/min (0.08 mg/g creatinine), and 2.04 ug/min (2.05 mg/g creatinine). The individual creatinine excretion rate was considerably influenced by sex, body wt, and smoking habits, thus influencing the metabolite concn standardized in relation to creatinine. Thus, both metabolites are estimates of **toluene** exposure; o-cresol is more specific than hippuric acid, but the individual variation in excretion of both metabolites is large, and when implementing either of them as biological exposure indexes, the influence of sex, body size, age as well as consumption of tobacco and alcohol has to be considered.
[Baelum J et al; Int Arch Occup Environ Health 59 (3): 281-94 (1987)]**PEER REVIEWED**

The distribution of radioactivity in pregnant mice was registered at different time intervals (0-24 hr) after a 10 min period of inhalation of **toluene**. ... Autoradiographic and liq scintillation methods were used to make possible the distinction between volatile, water sol, and firmly tissue bound radioactivity. **Toluene** reached high concns immediately after inhalation in lipid rich tissues (brain and fat) and well perfused organs (liver and kidney) but were rapidly eliminated resulting in low concns at 1 hr in all maternal tissues, except fat. Metabolites reached peak levels around 30 min to 1 hr after inhalation, but were also relatively rapidly eliminated. ... One exception was the very strong accumulation of water sol metabolites at 4 and 24 hr in the nasal mucosa and olfactory bulb after inhalation of **toluene**. Volatile radioactivity was observed in the placenta and fetuses immediately and up to 1 hr after inhalation of solvent at all stages of gestation. The fetal levels were, however, much lower than in maternal tissues. In early gestation, an even distribution pattern was observed, while the fetal liver reached a higher concn than other fetal tissues in late gestation. In similarity with maternal tissues, fetal tissues reached the highest levels of metabolites 30 min to 1 hr after inhalation. A retention in uterine fluid was seen at 4 hr. Otherwise no retention of metabolites was observed in the fetoplacental unit. No firmly tissue bound metabolites of the studied solvents were observed in the fetal tissues in late gestation, indicating no fetal capacity for formation of reactive metabolites.
[Ghantous H, Danielson BRG; Biol Res Pregnancy Perinatol 7 (3): 98-105 (1986)]**PEER REVIEWED**

A study was instituted to determine whether gavage dosing and inhalation exposure resulted in similar blood levels of **toluene**. Groups of male Sprague-Dawley rats were dosed with **toluene** either by gavage with 0.10, 0.25, 0.50, or 1.0 mg/kg/body weight or through exposure to atmospheres containing 200 to

1000 ppm **toluene**. Blood samples were taken at 0.5, 1.0, 2.0, 4.0, 6.0, and 24.0 hours following dosing. Steady state blood concentrations were reached for both inhaled doses within 30 minutes of the exposure. After 6 hours the steady state **toluene** blood concentrations for the 200 and 1000 ppm dose levels were 2.89 and 37.23 ppm, respectively. For the oral doses, the peak blood **toluene** concentration increased with increasing dosage. Blood profiles from higher oral doses more closely approximated the steady state inhalation blood profiles. At 24 hours following dosing, blood **toluene** levels from all doses by either route were below detectable levels, suggesting minimal carry over of **toluene** concentrations from one day to the next. An equation was derived which will allow the gavage dose of **toluene** to be made equivalent to an inhalation dose. Based on results of other studies, it was suggested that blood **toluene** levels following sc injection more closely resemble those obtained following inhalation than do blood levels after gavage. However, it is possible to obtain blood concentrations of **toluene** similar to those generated by a 6 hour inhalation exposure to 1000 ppm through gavage dosing.
[Sullivan MJ, Conolly RB; Environ Research 45 (1): 64-70 (1988)]**PEER REVIEWED**

An investigation was carried out to quantitate the effect of pulmonary ventilation on uptake and biological concentrations of six organic solvents. Tested solvents were acetone, styrene, **toluene**, xylenes, methylchloroform, and tetrachloroethylene. Lung uptake and urinary concentration (Cu) were measured in 15 volunteers, 24 to 52 years old, exposed in a chamber for 2 or 4 hours at rest, 2 hours with three alternations of light exercise, 1 hour of light exercise, or 30 minutes or more strenuous exercise. Environmental levels and urinary concentration were measured in 528 occupationally exposed workers before and after 4 hours of work at a light task (pulmonary ventilation 12 to 18 liters per minute). For volunteers, uptake and urinary concentration values were significantly correlated. Environmental levels and urinary concentration showed a close relationship for occupational exposure. Biological equivalent exposure limits corresponding to threshold limit value (TLV) time weighted averages were derived from urinary concentration values. For acetone, styrene, and xylenes, uptake for a given time and exposure level was dependent only on ventilation. The **toluene** retention index was slightly lower for exercise than for rest, and uptake was ventilation dependent during rest and ventilation and retention index dependent during exercise. Retention indices decreased with increasing ventilation at rest and during exercise for tetrachloroethylene and methylchloroform. Their urinary concentration values were ventilation and retention index dependent. Methylchloroform uptake was higher during light versus heavy exercise. It was concluded that work load profoundly affects the absorbed amount of chemical and should be a factor in implementation of biological exposure indices and TLVs.
[Pezzagno G et al; Am Ind Hygiene Assoc J 49 (11): 546-52 (1988)]**PEER REVIEWED**

Animal studies indicate that **toluene** readily crosses the placenta.
[Ellenhorn, M.J., S. Schonwald, G. Ordog, J. Wasserberger. Ellenhorn's Medical Toxicology: Diagnosis and Treatment of Human Poisoning. 2nd ed. Baltimore, MD: Williams and Wilkins, 1997. 166]**PEER REVIEWED**

When dogs were exposed to 0.4-0.6 ug/ml **toluene** vapor, 91-94% was taken up in the lungs. Absorption was complete when **toluene** was given orally to dogs; the blood level in rats increased more slowly after oral administration than after inhalation. Absorption through the skin of mice in vivo was 4.50 ug/sq cm per hour. **Toluene** penetrated rat skin excised three days after clipping and depilation with cream at a rate one-tenth that of benzene and ten times that of ortho-xylene.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of

Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47 93 (1989)]**PEER REVIEWED**

Toluene levels in brain and blood were linearly related to **toluene** levels in inhaled air after rats were exposed to 50, 100, 500, or 1000 ppm (189, 377, 1885, or 3770 mg/cu m) **toluene** for 3 hr.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47 93 (1989)]**PEER REVIEWED**

When rabbits were given a single oral dose of 350 mg/kg bw **toluene**, 19% was exhaled unchanged within 12 hr.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47 94 91989)]**PEER REVIEWED**

Pregnant C57B1 mice were exposed by inhalation to 14C-**toluene** (theoretical concentration, 2000 ppm (7540 mg/cu m)) for 10 min on days 11, 14 or 17 of gestation, and distribution of the label was determined 0, 0.5, 1, 4 and 24 hr after exposure. The label quickly entered the embryo, but uptake was low relative to that in maternal tissues. All fetal activity was extractable, indicating that no firmly bound metabolite was present.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47 94 (1989)]**PEER REVIEWED**

In humans, up to 75% of inhaled **toluene** is metabolized to hippuric acid and excreted in the urine within 12 hr of exposure. The remainder of the **toluene** is mainly excreted unchanged with a small percent being excreted as a sulfate or glucuronide of cresol.
[Sullivan, J.B. Jr., G.R. Krieger (eds.). Hazardous Materials Toxicology-Clinical Principles of Environmental Health. Baltimore, MD: Williams and Wilkins, 1992. 1091]**PEER REVIEWED**

The uptake of **toluene** in the blood is doubled during physical activity compared to the uptake at rest.
[Zenz, C., O.B. Dickerson, E.P. Horvath. Occupational Medicine. 3rd ed. St. Louis, MO., 1994 723]**PEER REVIEWED**

In nude mice exposure to 300, 1000, or 3000 ppm **toluene** under conditions where there was no respiratory intake of **toluene**, led to a dose-related and duration-related increase in whole body **toluene** levels. The calculated skin absorption coefficient was 1.24 cm/hr. The skin absorption rate for the 300 ppm concentration was 0.0009 mg/sq cm/hr; for the 1000 ppm concentration , it was 0.0046 mg/sq cm/hr; and for the 3000 ppm concentration, it was 0.0144 mg/sq cm/hr.
[Tsuruta H; Ind Health 27: 37-47 (1989) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.68 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

In humans, the **toluene** is distributed between the plasma and red blood cells at approximately a 1:1 ratio according to in vitro data; in rats, the ratio is 1:2 based on in vivo data.
[Lam CW et al; Toxicol Appl Pharmacol 104: 117-29 (1990) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.68 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

In one human who died 30 min after ingestion of 625 mg/kg **toluene**, the liver was found to have the highest concentration of **toluene** (133.5 ug/g) followed by the pancreas (88.2 ug/g), brain (85.3 ug/g), heart (62.6 ug/g), blood (12.2 ug/g), body fat (12.2 ug/g), and cerebrospinal fluid (11.1 ug/g).
[Ameno K et al; Forensic Sci Int 41: 255-60 (1989) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.71 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

Biological Half-Life:

0.083 days (Inhaled as environmental air)
[Cleland, J.G., G.L. Kingsbury. Multimedia Environmental Goals for Environmental Assessment. Volume 1. EPA-600/7-77-136a. Research Triangle Park, NC: EPA, Nov. 1977.,p. E-146]**PEER REVIEWED**

Mechanism of Action:

... **Toluene** at low concn /less than 100 ppm/ may produce disturbances in dopaminergic mechanisms of the basal ganglia probably leading to functional changes in sensory-motor integration. ...
[Fuxe K et al; Toxicol Lett 12 (2-3): 115-23 (1982)]**PEER REVIEWED**

Exposure to **toluene** causes both reversible and irreversible changes in the central nervous system. The effects of **toluene** inhalation on some specific enzymes and glutamate and GABA receptor binding in defined parts of the rat brain were studied following several exposure schemes. The activities of the transmitter synthesizing enzymes glutamic acid decarboxylase (GAD), choline acetyltransferase (ChAT) and aromatic amino-acid decarboxylase (AAD) were used as markers for permanent loss of neuronal activity. Catecholaminergic neurons showed a 50% reduction in the brain stem after 4 weeks exposure to 250 and 1000 ppm **toluene**. Following 500 ppm of **toluene**, 16 hr/day for 3 months, a general increase in the activities was seen. This is most probably due to a reduction in total protein content, to which the activities were related. The neurotransmitters glutamate and GABA had their specific receptor binding increased in most of the brain areas studied, but decreased in some areas. The glial enzyme, glutamine synthetase, has its activity increased in the cerebellar hemisphere following 4 weeks exposure to 1000 ppm. This suggests that glial cells in the area may have proliferated, a frequent phenomenon following CNS damage.
[Bjornaes S, Naalsund Lu; Toxicol 49 (2-3): 367-74 (1988)]**PEER REVIEWED**

The effect of styrene, **toluene**, ethylbenzene, alpha-methylstyrene, and butylbenzene on oxidative phosphorylation was studied using rat liver mitochondrial preparations. Rat liver mitochondria were prepared from male white Wistar rats and assessed for respiration rate, oxygen uptake, glutamate oxidation, succinate oxidation, ATPase activity, and proton permeability in the presence and absence of

the alkyl benzene derivatives. Inclusion of the alkyl benzene derivatives in the incubation medium produced an initial acceleration of oxygen consumption followed by an inhibition of glutamate oxidation, and the stimulatory effect paralleled the aliphatic chain length. Glutamate oxidation was also inhibited by styrene, ethylbenzene, and alpha-methylstyrene but not by butylbenzene or **toluene** in 2,4-dinitrophenol uncoupled mitochondria. Styrene and the aliphatic benzene derivative stimulated succinate oxidation in rat liver mitochondria without effect on 2,4-dinitrophenol stimulated succinate oxidation. Similar stimulatory effects on ATPase activity were observed with maximal stimulation occurring at the same relative concentrations producing maximal succinate oxidation. ATPase stimulation required magnesium, was oligomycin sensitive, and showed an inverse relation to the hydrophobicity of the compounds tested. The inclusion of styrene in the incubation medium markedly increased the rate of passive entry of protons into rat liver mitochondria in a manner comparable to 2,4-dinitrophenol. It was concluded that styrene and other monosubstituted benzene derivatives act as mitochondrial uncoupling agents.
[Mickiewicz W, Rzeczycki W; Biochem Pharmacol 37 (23): 4439-44 (1988)]**PEER REVIEWED**

Interactions:

IP LD50 OF **TOLUENE** FOR MALE MICE WAS 1.15 G/KG. PRETREATMENT WITH PHENOBARBITAL, PRODUCED MARKED DECR IN SLEEP INDUCED BY TEST DOSE (0.96 G/KG IP) OF **TOLUENE**. PRETREATMENT WITH HEPATIC ENZYME INHIBITORS SUCH AS CARBON TETRACHLORIDE, 2-DIETHYLAMINOETHYL-2,2-DIPHENYLATE HYDROCHLORIDE, PYRAZOLE & CYANAMIDE PRODUCED INCR IN SLEEP & DEATH ASSOC WITH PROLONGATION OF SLEEPING TIME.
[KOGA K, OHMIYA Y; J TOXICOL SCI 3 (1): 25 (1978)]**PEER REVIEWED**

TOLUENE WITH ASPHALT FUMES OR CHLORINATED HYDROCARBONS, SUCH AS TRICHLOROETHYLENE & TETRACHLOROETHENE, CAUSES DEPRESSION OF HYDROXYLATION & URINARY CONJUGATE EXCRETIONS. ... COMBINED EXPOSURE TO **TOLUENE**, XYLENE, FORMALDEHYDE, & ANILINE DYES DECR GRANULOCYTIC PHOSPHATASE ACTIVITY. CONVERSELY, HYDROGEN PEROXIDE ADMIN TO RATS INCR THE BLOOD PEROXIDE ACTIVITY & INCR THE TOLERANCE TO **TOLUENE**, AS DID PHENOBARBITAL IN SPECIFIC QUANTITIES.
[Clayton, G. D. and F. E. Clayton (eds.). Patty's Industrial Hygiene and Toxicology: Volume 2A, 2B, 2C: Toxicology. 3rd ed. New York: John Wiley Sons, 1981-1982. 3289]**PEER REVIEWED**

SPRAGUE-DAWLEY RATS WERE EXPOSED BY INHALATION TO **TOLUENE** (500, 1500, & 3000 PPM) FOR 3 DAYS. **TOLUENE** INCR CONCN OF LIVER MICROSOMAL CYTOCHROME P-450. A DOSE-DEPENDENT INCR IN THE IN VITRO LIVER MICROSOMAL FORMATION OF SEVERAL METABOLITES OF BIPHENYL & BENZO(A)PYRENE WAS OBSERVED FOR **TOLUENE**. **TOLUENE** MODIFIED THE METABOLISM AND TOXICITY OF OTHER ENVIRONMENTAL CONTAMINANTS.
[TOFTGARD R ET AL; ACTA PHARMACOL TOXICOL 51 (2): 108 (1982)]**PEER REVIEWED**

Perchloroethylene enhances toxicity of **toluene** admin orally in rats.
[USEPA; Health Assessment Document: Toluene p.15-1 (1982)

EPA-800/8-82-008]**PEER REVIEWED**

Toluene and trichloroethylene seem to exhibit competitive inhibition.
[Ikeda M; Int Arch Arbeitsmed 33 (2): 125 (1974)]**PEER REVIEWED**

CFY rats ... on day 12 of pregnancy ... dams were given: 0, 125, 250, 500 and 3,600 mg/cu m ... and 250 mg/kg acetylsalicylic acid by gavage; two subgroups ... treated with 250 mg/kg acetylsalicylic acid in combination with 3,600 mg/cu m **toluene** inhalation were given 0, 2.5, or 5 gm/kg glycine 2 hours before the acetylsalicylic acid dose. ... **Toluene** was found to potentiate the toxic effect of acetylsalicylic acid and to increase both maternal and embryonic toxicity ... increasing acetylsalicylic acid embryotoxicity caused by **toluene** can be warded off by glycine administration.
[Ungvary G et al; Teratology 27 (2): 261-9 (1983)]**PEER REVIEWED**

The metabolic interaction of **toluene** and ethanol was studied in male rabbits having received ethanol (26.0 mmol/kg po), **toluene** (5.4 mmol/kg po) or both. Compared with ethanol alone, **toluene** given 2 hr after ethanol caused a significantly higher and more prolonged concentration of blood alcohol. A similar trend of blood alcohol was observed at the later stage with **toluene** given prior to ethanol. On the other hand, with simultaneous doses of the two substances, the blood **toluene** concentration was higher for the first 15-30 min than the ethanol control and the urinary excretion of hippuric acid, a main metabolite of **toluene**, was markedly decreased for the first 2 hr. The blood ethanol in this group, on the contrary, was reduced until 1 hr after administration. These results indicate that **toluene** and ethanol act reciprocally as competitive inhibitors in their metabolism after single administrations.
[Takahashi S et al; Arch Toxicol 59 (5): 307-10 (1987)]**PEER REVIEWED**

In an experimental human study, the effect of **toluene** and ethanol (alone or in combination) on psychophysiologic functions was studied in 12 men (22-44 yr of age). Each subject served as his own control. Subjects were exposed to **toluene** by inhalation at a concentration of 300 mg **toluene**/cu m air for 4.5 hr. Ethanol was ingested at a dose equivalent to 15 mmol ethanol/kg body weight. **Toluene** had no significant effect on the 4 performance tests. A significant but weak depression of heart rate was observed during sleep latency tests (1-2.5 beats/min, 0.001 <p< 0.01). There was a significant increase in reporting of headache (p< 0.05) and in reporting for all symptoms (nausea, headache, irritation) combined (p< 0.05). No interaction between ethanol and **toluene** was observed.
[Iregren A et al; Scand J Work Environ Health 12: 128-36 (1986)]**PEER REVIEWED**

Male Sprague-Dawley rats were used to study the renal toxicity potential of subchronic exposure to non-toxic doses of a combination of styrene and **toluene**. Four groups (n= 6) of rats were injected ip with: (1) 4 mmol styrene 2 times/day at 4 hr intervals; (2) 10 mmol **toluene**/kg once a day; (3) 4 mmol styrene/kg 2 times/day plus 10 mmol **toluene**/kg once/day; (4) All treatments were given 5 days/wk for 4 consecutive wk. By the fourth wk, there was a significant increase (p< 0.05) in urinary excretion of gamma-glutamyl transpeptidase, protein, and glucose by the group receiving combined treatment versus those receiving treatment with either chemical alone. There was an increase in excretion of hippuric acid in the mixture treatment group, but no increase in mandelic and phenylglyoxylic acids or thioethers. Blood urinary nitrogen was not modified by the individual chemicals or the mixture. Electron microscopic examination of the kidney showed an increase of single membrane vacuoles in the proximal convoluted tubules of rats treated with a mixture of chemicals, but not with **toluene** or styrene alone.

[Chakrabarti S, Tuchweber B; Toxicol Lett 39 (1): 27-34 (1987)]**PEER REVIEWED**

... **Toluene** has been shown to be a competitive inhibitor of the metabolism of benzene. This competitive interaction alleviates the metabolite-mediated toxicity of benzene ...
[Klaassen, C.D., M.O. Amdur, Doull J. (eds.). Casarett and Doull's Toxicology. The Basic Science of Poisons. 5th ed. New York, NY: McGraw-Hill, 1995. 741]**PEER REVIEWED**

Xenobiotic competitors for the same metabolic route, such as benzene and xylene, would ... have an impact on **toluene** metabolism.
[U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.95 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

... A single alcoholic drink has a very strong, acute inhibitory effect on the hepatic elimination of **toluene**.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V71 842 (1999)]**PEER REVIEWED**

The aim of this study was to examine if the drug chlorzoxazone has any influence on the toxicokinetics of acetone and **toluene**. Chlorzoxazone is mainly metabolized by the same enzyme (Cytochrome P450 2E1) as ethanol and many other organic solvents. Ten male volunteers were exposed to solvent vapor (2 hr, 50 watt) in an exposure chamber. Each subject was exposed to acetone only (250 ppm), acetone + chlorzoxazone, **toluene** (50 ppm) only, **toluene** + chlorzoxazone, and chlorzoxazone only. Chlorzoxazone (500 mg) was taken as two tablets 1 h prior to solvent exposure. Samples of blood, urine and exhaled air were collected before, during and until 20 h post exposure. The time-concentration curves of acetone and **toluene** in blood were fitted to one- and four-compartment toxicokinetic models, respectively. Except for a delayed excretion of hippuric acid in urine, no effects on the **toluene** toxicokinetics were seen after chlorzoxazone treatment. Small increases in chlorzoxazone plasma levels were seen after exposure compared to chlorzoxazone alone. These interactions, although statistically significant, seem to be small compared to the interindividual variability on metabolism and toxicokinetics.
[Ernstgard L et al; Toxicol Sci 48 (2): 189-96 (1999)]**PEER REVIEWED**

Pharmacology:

Interactions:

IP LD50 OF **TOLUENE** FOR MALE MICE WAS 1.15 G/KG. PRETREATMENT WITH PHENOBARBITAL, PRODUCED MARKED DECR IN SLEEP INDUCED BY TEST DOSE (0.96 G/KG IP) OF **TOLUENE**. PRETREATMENT WITH HEPATIC ENZYME INHIBITORS SUCH AS CARBON TETRACHLORIDE, 2-DIETHYLAMINOETHYL-2,2-DIPHENYLATE HYDROCHLORIDE, PYRAZOLE & CYANAMIDE PRODUCED INCR IN SLEEP & DEATH ASSOC WITH PROLONGATION OF SLEEPING TIME.

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The metabolic interaction of **toluene** and ethanol was studied in male rabbits having received ethanol (26.0 mmol/kg po), **toluene** (5.4 mmol/kg po) or both. Compared with ethanol alone, **toluene** given 2 hr after ethanol caused a significantly higher and more prolonged concentration of blood alcohol. A similar trend of blood alcohol was observed at the later stage with **toluene** given prior to ethanol. On the other hand, with simultaneous doses of the two substances, the blood **toluene** concentration was higher for the first 15-30 min than the ethanol control and the urinary excretion of hippuric acid, a main metabolite of **toluene**, was markedly decreased for the first 2 hr. The blood ethanol in this group, on the contrary, was reduced until 1 hr after administration. These results indicate that **toluene** and ethanol act reciprocally as competitive inhibitors in their metabolism after single administrations.
[Takahashi S et al; Arch Toxicol 59 (5): 307-10 (1987)]**PEER REVIEWED**

In an experimental human study, the effect of **toluene** and ethanol (alone or in combination) on psychophysiologic functions was studied in 12 men (22-44 yr of age). Each subject served as his own control. Subjects were exposed to **toluene** by inhalation at a concentration of 300 mg **toluene**/cu m air for 4.5 hr. Ethanol was ingested at a dose equivalent to 15 mmol ethanol/kg body weight. **Toluene** had no significant effect on the 4 performance tests. A significant but weak depression of heart rate was observed during sleep latency tests (1-2.5 beats/min, 0.001 <p< 0.01). There was a significant increase in reporting of headache (p< 0.05) and in reporting for all symptoms (nausea, headache, irritation) combined (p< 0.05). No interaction between ethanol and **toluene** was observed.
[Iregren A et al; Scand J Work Environ Health 12: 128-36 (1986)]**PEER REVIEWED**

Male Sprague-Dawley rats were used to study the renal toxicity potential of subchronic exposure to non-toxic doses of a combination of styrene and **toluene**. Four groups (n= 6) of rats were injected ip with: (1) 4 mmol styrene 2 times/day at 4 hr intervals; (2) 10 mmol **toluene**/kg once a day; (3) 4 mmol styrene/kg 2 times/day plus 10 mmol **toluene**/kg once/day; (4) All treatments were given 5 days/wk for 4 consecutive wk. By the fourth wk, there was a significant increase (p< 0.05) in urinary excretion of gamma-glutamyl transpeptidase, protein, and glucose by the group receiving combined treatment versus those receiving treatment with either chemical alone. There was an increase in excretion of hippuric acid in the mixture treatment group, but no increase in mandelic and phenylglyoxylic acids or thioethers. Blood urinary nitrogen was not modified by the individual chemicals or the mixture. Electron microscopic examination of the kidney showed an increase of single membrane vacuoles in the proximal convoluted tubules of rats treated with a mixture of chemicals, but not with **toluene** or styrene alone.
[Chakrabarti S, Tuchweber B; Toxicol Lett 39 (1): 27-34 (1987)]**PEER REVIEWED**

... **Toluene** has been shown to be a competitive inhibitor of the metabolism of benzene. This competitive interaction alleviates the metabolite-mediated toxicity of benzene ...
[Klaassen, C.D., M.O. Amdur, Doull J. (eds.). Casarett and Doull's Toxicology. The Basic Science of Poisons. 5th ed. New York, NY: McGraw-Hill, 1995. 741]**PEER REVIEWED**

Xenobiotic competitors for the same metabolic route, such as benzene and xylene, would ... have an impact on **toluene** metabolism.
[U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.95 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

... A single alcoholic drink has a very strong, acute inhibitory effect on the hepatic elimination of **toluene**.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V71 842 (1999)]**PEER REVIEWED**

The aim of this study was to examine if the drug chlorzoxazone has any influence on the toxicokinetics of acetone and **toluene**. Chlorzoxazone is mainly metabolized by the same enzyme (Cytochrome P450 2E1) as ethanol and many other organic solvents. Ten male volunteers were exposed to solvent vapor (2

hr, 50 watt) in an exposure chamber. Each subject was exposed to acetone only (250 ppm), acetone + chlorzoxazone, **toluene** (50 ppm) only, **toluene** + chlorzoxazone, and chlorzoxazone only. Chlorzoxazone (500 mg) was taken as two tablets 1 h prior to solvent exposure. Samples of blood, urine and exhaled air were collected before, during and until 20 h post exposure. The time-concentration curves of acetone and **toluene** in blood were fitted to one- and four-compartment toxicokinetic models, respectively. Except for a delayed excretion of hippuric acid in urine, no effects on the **toluene** toxicokinetics were seen after chlorzoxazone treatment. Small increases in chlorzoxazone plasma levels were seen after exposure compared to chlorzoxazone alone. These interactions, although statistically significant, seem to be small compared to the interindividual variability on metabolism and toxicokinetics.
[Ernstgard L et al; Toxicol Sci 48 (2): 189-96 (1999)]**PEER REVIEWED**

Minimum Fatal Dose Level:

Ingestion of approximately 60 ml (625 mg/kg) of **toluene** proved fatal for a while male mental patient.
[Ameno K et al; Forensic Sci Int 41: 255-60 (1989) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.52 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

Environmental Fate & Exposure:

Environmental Fate/Exposure Summary:

Toluene is released into the atmosphere principally from the volatilization of petroleum fuels and **toluene**-based solvents and thinners and from motor vehicle exhaust. **Toluene**'s production and use as an intermediate in the production of benzoic acid, benzaldehyde, benzene, explosives, dyes and many other organic compounds may also result in its release to the environment through various waste streams. **Toluene** has been detected in emissions from volcanos, forest fires and crude oil. If released to air, a vapor pressure of 28.4 mm Hg at 25 deg C indicates **toluene** will exist solely as a vapor in the ambient atmosphere. Vapor-phase **toluene** will be degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals; the half-life for this reaction in air is estimated to be 3 days. **Toluene** may also be degraded in the atmosphere by reaction with nitrate radicals and ozone molecules, but these reactions are too slow to be environmentally important. If released to soil, **toluene** is expected to have high to moderate mobility based upon Koc values in the range of 37-178. Volatilization from moist soil surfaces is expected to be an important fate process based upon a Henry's Law constant of 6.64X10-3 atm-cu m/mole. **Toluene** may volatilize from dry soil surfaces based upon its vapor pressure. Biodegradation is expected to occur rapidly in soil surfaces, with half-lives in the range of several hours to 71 days. If released into water, **toluene** is not expected to adsorb to suspended solids and sediment based upon a Koc of 166 measured in lake sediment. Biodegradation is expected to occur rapidly in water, with reported half-lives of 4 and 56 days in aerobic and anaerobic water, respectively. Volatilization from water surfaces is expected to be an important fate process based upon this compound's Henry's Law constant. Estimated volatilization half-lives for a model river and model lake are 1 hour and 4 days, respectively. Measured BCF values of 13 and 90 in fish suggest bioconcentration in aquatic organisms is low to moderate. Hydrolysis is not expected to be an important environmental fate process for **toluene** due to lack of hydrolyzable functional groups. Exposure to **toluene** may occur

occupationally during its production or subsequent use, particularly as a solvent or in gasoline, via dermal and respiratory routes. The main route of exposure for the general population will be through inhalation from contaminated air and handling of gasoline as well as ingestion of contaminated drinking water and food, and exposure to some consumer products. (SRC)
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Probable Routes of Human Exposure:

NIOSH (NOES Survey 1981-1983) has statistically estimated that 1,625,598 workers (288,299 of these are female) are potentially exposed to **toluene** in the US(1). Occupational exposure to **toluene** may occur through inhalation and dermal contact with this compound at workplaces where **toluene** is produced or used(SRC). The general population may be exposed to **toluene** via inhalation of ambient air, ingestion of food and drinking water, handling of gasoline, and exposure to some consumer products where **toluene** is used as a solvent(SRC).
[(1) NIOSH; National Occupational Exposure Survey (NOES) (1983)]**PEER REVIEWED**

Toluene was detected in hairdresser salons in Norway at concns of 0.04-0.11 mg/cu m(1). The time weighted average (TWA) of **toluene** in the workplace air of a municipal waste composting facility was reported as 188,000 ug/cu m(2). In a 1989 Danish survey on chemical exposures(3), the number of worker exposure events for **toluene** were documented: manufacturing of metals, 420; manufacturing of metal fabricated products 64,000; electrical machinery and apparatus, 1,500; manufacture of transport equipment 2,700; painters and carpenters 15,000; construction workers, 5,400; publishing and printing, 6,300; wholesale trades, 5,000; textile and leather manufacturing, 4,400; wood and furniture manufacturing, 5,900; manufacture of chemicals, 8,700; manufacture of paints and petroleum, 1,400; manufacture of non-metallic mineral products, 2,300; manufacture of optical instruments, 2,500 manufacture of plastic and boat building, 1,100; sewage and refuse disposal, 99; agriculture and forestry, 11,000; health services, 2,600. The total number of work related exposure events was 140,000(3). **Toluene** was detected in the workplace air of glass fiber manufacturing plants and high temperature sealing component and clutch lining plants at a mean concn of 65 ppm(4).
[(1) Hollund BE, Moen BE; Ann Occup Hyg 42: 277-81 (1998) (2) Eitzer BD; Environ Sci Technol 29: 896-902 (1995) (3) Brandorff NP et al; Occup Environ Med 52: 454-63 (1995) (4) Angerer J, Kraemer A; Int Arch Occup Environ Health 69: 91-96 (1997)]**PEER REVIEWED**

Body Burden:

Toluene was identified, not quantified, in 8 samples of mothers' milk from 4 urban areas(1). **Toluene** was detected in 250 of 250 specimens of human blood at concns of 0.2-38 ppb (1.5 ppb avg)(2). **Toluene** was detected in 91% of the samples of the National Human Adipose Tissue Survey at a max concn of 250 ppb(3). **Toluene** was identified, not quantified, in expired breath of people at service stations during fueling(4). The mean concn of **toluene** in the blood of non-occupationally exposed individuals in the US was 0.52 ppb(5). The avg concn of **toluene** in the blood and urine of workers in glass fiber and clutch lining plants were 911 ug/l and 2.9 mg/l, respectively(6).
[(1) Pellizzari ED et al; Bull Environ Contam Toxicol 28: 322-8 (1982) (2) Antoine SR et al; Bull Environ Contam Toxicol 36: 364-71 (1986) (3) Stanley JS; Broad Scan Analysis of the FY82 National Human Adipose

Tissue Survey Specimens Vol. I Executive Summary p. 5 USEPA-560/5-86-035 (1986) (4) Lindstrom AB, Pleil J; J Air Waste Manage Assoc 46: 676-82 (1996) (5) Ashley DL et al; Clin Chem 40: 1401-14 (1994) (6) Angerer J, Kraemer A; Int Arch Occup Environ Health 69: 91-96 (1997)]**PEER REVIEWED**

Average Daily Intake:

AIR INTAKE (assume median concn 11 ppb(1)) 843 ug; WATER INTAKE (assume 2 ppb(2)) 4 ug; FOOD INTAKE - insufficient data.
[(1) Brodzinsky R, Singh HB; Volatile Organics in the Atmosphere and Assessment of available data: p. 126-7 SRI Contract 68-02-3459 (1982) (2) Otson R et al; J Assoc Off Analyt Chem 65: 1370-4 (1982)]**PEER REVIEWED**

Natural Pollution Sources:

Toluene occurs in nature in ... natural gas deposits ...
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47 82 (1989)]**PEER REVIEWED**

Toluene has been detected in emissions from volcanos, forest fires and crude oil(1).
[(1) Graedel TE; Chemical Compounds in the Atmosphere, NY, NY, Academic Press p. 108 (1978)]**PEER REVIEWED**

Artificial Pollution Sources:

Toluene is a major constituent (20-60 ug/cigarette) of the gas phase of the mainstream smoke of unfiltered cigarettes. /From table/
[Rom, W.N. (ed.). Environmental and Occupational Medicine. 2nd ed. Boston, MA: Little, Brown and Company, 1992. 1212]**PEER REVIEWED**

Toluene is released into the atmosphere principally from the volatilization of petroleum fuels and **toluene**-based solvents and thinners and from motor vehicle exhaust(1,2). **Toluene**'s production and use as an intermediate in the production of benzoic acid, benzaldehyde, explosives, dyes and many other organic compounds(3) may also result in its release to the environment through various waste streams(SRC).
[(1) Graedel TE; Chemical Compounds in the Atmosphere. NY, NY: Academic Press p. 108 (1978) (2) Walker P; Air Pollution Assessment of Toluene. TR-7215 Mitre Corp, McLean VA, pp. 1-22, 46-92 (1976) (3) Budvari S; Merck Index, 12th ed, Whitehouse Station, NJ Merck & Co. p 1626 (1996)]**PEER REVIEWED**

Environmental Fate:

TERRESTRIAL FATE: Based on a classification scheme(1), Koc values of 37-178 measured in soil(2,3), indicates that **toluene** is expected to have high to moderate mobility in soil(SRC).

Volatilization of **toluene** from moist soil surfaces is expected to be an important fate process(SRC) given a Henry's Law constant of 6.64X10-3 atm-cu m/mole(4). **Toluene** may volatilize from dry soil surfaces based on a vapor pressure of 28.4 mm Hg at 25 deg C(5). Complete biodegradation of **toluene** was observed in lab microcosm tests during a 40 hour incubation period using soils previously exposed to **toluene**(6). The biodegradation half-life in various soils was reported as several hours to 71 days(7).
[(1) Swann RL et al; Res Rev 85: 17-28 (1983) (2) Wilson JT et al; J Environ Qual 10: 501-6 (1981) (3) Nathwani JS, Phillips CR; Chemosphere 6: 157-62 (1977) (4) Mackay D et al; Environ Sci Technol 13: 333-36 (1979) (5) Daubert TE, Danner RP; Physical and Thermodynamic Properties of Pure Chemicals Data Compilation Washington, DC: Taylor and Francis (1989) (6) Allen-King RM et al; Environ Toxicol Chem 13: 693-705 (1994) (7) Aronson D et al; Aerobic biodegradation of organic chemicals in environmental media: a summary of field and laboratory studies. USEPA (1999)]**PEER REVIEWED**

AQUATIC FATE: Based on a classification scheme(1), a Koc value of 166 measured in lake sediment(2) indicates that **toluene** is not expected to adsorb to suspended solids and sediment(SRC). Volatilization from water surfaces is expected(3) based upon a Henry's Law constant of 6.64X10-3 atm-cu m/mole(4). Using this Henry's Law constant and an estimation method(3), volatilization half-lives for a model river and model lake are 1 hour and 4 days, respectively(SRC). According to a classification scheme(5), BCF values of 13(6) and 90(7) measured in fish, suggest bioconcentration in aquatic organisms is low to moderate. The half-life of **toluene** in aerobic and anaerobic water was reported as 4 and 56 days, respectively(8).
[(1) Swann RL et al; Res Rev 85: 17-28 (1983) (2) Kan AT et al; Environ Sci Technol 32: 892-902 (1998) (3) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington, DC: Amer Chem Soc pp. 4-9, 15-1 to 15-29 (1990) (4) Mackay D et al; Environ Sci Technol 13: 333-36 (1979) (5) Franke C et al; Chemosphere 29: 1501- 14 (1994) (6) Ogata M, Miyake Y; Water Res 12: 1041-4 (1978) (7) Freitag D et al; Chemsophere 14: 1589-1616 (1985) (8) Capel PD, Larson SL; Chemosphere 30: 1097-1107 (1995)]**PEER REVIEWED**

ATMOSPHERIC FATE: According to a model of gas/particle partitioning of semivolatile organic compounds in the atmosphere(1), **toluene**, which has a vapor pressure of 28.4 mm Hg at 25 deg C(2), is expected to exist solely as a vapor in the ambient atmosphere. Vapor-phase **toluene** is degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals, nitrate radicals and ozone molecules(SRC). The half-life for the reaction with hydroxyl radicals is estimated to be 3 days(SRC), calculated from its rate constant of 5.96X10-12 cu cm/molecule-sec at 25 deg C(3). The half-life for the nighttime reaction with nitrate radicals is estimated as 491 days(SRC) calculated from its rate constant of 6.8X10-17 cu cm/molecule-sec at 25 deg C(3). The half-life for the reaction with ozone is estimated as 27,950 days(SRC) calculated from its rate constant of 4.1X10-22 cu cm/molecule-sec at 25 deg C(3).
[(1) Bidleman TF; Environ Sci Technol 22: 361-367 (1988) (2) Daubert TE, Danner RP; Physical and Thermodynamic Properties of Pure Chemicals Data Compilation Washington, DC: Taylor and Francis (1989)(3) Atkinson R; J Phys Chem Ref Data Monograph 2 (1994)]**PEER REVIEWED**

Environmental Biodegradation:

Toluene is readily degradable in a variety of standard biodegradability tests using sewage seed or sludge inoculums(1-7). Degradation has been observed in several die-away tests using seawater or estuarine water(9-12). The degradation rate is much faster in systems which have been contaminated by oil(9,10). Complete degradation has been observed in 4 days and 22 days in a marine mesocosm with summer and spring conditions, respectively(12), and 10 days in a 1% gas oil mixture in a North Sea coast water inoculum(8). A 90 day half-life in uncontaminated estuarine water was reduced to 30 days in oil-polluted water(10). The half-life in water collected near Port Valdez, Alaska was 12 days(9). 1.5 mM and 3 mM Ring-labeled **toluene** added to a methanogenic inoculum originally enriched from sewage sludge and incubated at 35 deg C for 60 days resulted in 3.6 and 4.5% 14-C final activity respectively(13).
[(1) Tabak HH et al; J Water Pollut Control Fed 53: 1503-8 (1981) (2) Davis EM et al; Water Res 15: 1125-7 (1981) (3) Bridie AL et al; Water Res 13: 627-30 (1979) (4) Kawasaki M; Ecotox Environ Safety 4: 444-54 (1980) (5) Malaney GW, McKinney RE; Water Sewage Works 113: 302-9 (1966) (6) Price KS et al; J Water Pollut Control Fed 46: 63-77 (1974) (7) Matsui S et al; Prog Water Technol 7: 645-59 (1975) (8) Van der Linden AC; Dev Biodegrad Hydrocarbons 1: 165-200 (1978) (9) Button DK et al; Appl Environ Microbiol 42: 708-19 (1981) (10) Lee RF; 1977 Oil Spill Conf Amer Petrol Inst p 611-6 (1977) (11) Reichardt PB et al; Environ Sci Technol 15: 75-9 (1981) (12) Wakeham SG et al; Environ Sci Technol 17: 611-7 (1983) (13) Grbic-Galic D, Vogel TM; Appl Environ Microbiol 53: 254-60 (1987)]**PEER REVIEWED**

Toluene completely degraded in groundwater in 8 days including a lag of 3-4 days while microbial populations became acclimated(1). Other investigators found that only 1-2% of **toluene** degraded in the subsurface environment(2) and >90% degraded in 4 weeks in soil cores at various depths both above and below the water table(3,5). Microbial attack proceeds via immediate hydroxylation of the benzene ring followed by ring-cleavage or oxidation of the side chain followed by hydroxylation and ring-cleavage(4).
[(1) Kappeler T, Wuhrmann K; Water Res 12: 327-33 (1978) (2) Wilson JT et al; Devel Indust Microbiol 24: 225-33 (1983) (3) McNabb JF et al; 81st Ann Mtg Amer Soc Microbiology p.213 (1981) (4) Fewson CA; FEMS Symp 12 (Microb Deg Xenobiotics Recalcitrant Cmpds): 141-79 (1981) (5) Wilson JT et al; Ground Water 21: 134-42 (1983)]**PEER REVIEWED**

Complete biodegradation of **toluene** was observed in lab microcosm tests during a 40 hour incubation period using soils previously exposed to **toluene**(1). **Toluene** was rapidly degraded in soil column experiments using acclimated soil at a rate of 8-35 mg/kg-day, and the rate followed zero-order kinetics(2). First-order degradation rate constants of 0.0005 to 0.0063 day-1 were measured for **toluene** in a gasoline-contaminated aquifer zone(3). These rate constants correspond to half-lives of 100-1,386 days(3). A first-order biodegradation rate constant of 0.045 day-1 was reported for **toluene** in an anaerobic petroleum contaminated aquifer, corresponding to a biodegradation half-life of 15 days(4). **Toluene** was rapidly biodegraded by indigenous mixed cultures in sandy aquifer material and pure cultures isolated from the aquifer(5). The zero-order rate constant for the aquifer material was 23 mg/l-day and had a lag period of 2 days(5). The half-life of **toluene** in aerobic and anaerobic water was reported as 4 and 56 days, respectively(6). The biodegradation half-life in various soils was reported as several hours to 71 days(7).
[(1) Allen-King RM et al; Environ Toxicol Chem 13: 693-705 (1994) (2)

Allen-King RM et al; J Environ Qual 25: 287-95 (1996) (3) Borden RC et al; Water Resour Res 33: 1105-15 (1997) (4) Borden RC et al; Anaerobic Biodegradation of BTEX in Aquifer Material USEPA/600/S-97/003. National Risk Management Laboratory, Ada, OK. pp. 9 (1997) (5) Alvarez PJJ, Vogel TM; Appl Environ Microbiol 57: 2981-85 (1991) (6) Capel PD, Larson SL; Chemosphere 30: 1097-1107 (1995) (7) Aronson D et al; Aerobic biodegradation of organic chemicals in environmental media: a summary of field and laboratory studies. USEPA (1999)]**PEER REVIEWED**

Environmental Abiotic Degradation:

The rate constant for the vapor-phase reaction of **toluene** with photochemically-produced hydroxyl radicals has been measured as 5.96X10-12 cu cm/molecule-sec at 25 deg C(1). This corresponds to an atmospheric half-life of about 3 days at an atmospheric concentration of 5X10+5 hydroxyl radicals per cu cm(1). The rate constant for the vapor-phase reaction of **toluene** with nitrate radicals has been measured as 6.8X10-17 cu cm/molecule-sec at 25 deg C(1). This corresponds to an atmospheric half-life of about 491 days at an atmospheric concentration of 2.4X10+8 nitrate radicals per cu cm(2). The rate constant for the vapor-phase reaction of **toluene** with ozone has been measured as 4.1X10-22 cu cm/molecule-sec at 25 deg C(1). This corresponds to an atmospheric half-life of about 27,950 days at an atmospheric concentration of 7X10+11 ozone molecules per cu cm(3). **Toluene** is not expected to undergo hydrolysis in the environment due to the lack of hydrolyzable functional groups(4) nor to directly photolyze due to the lack of absorption in the environmental UV spectrum.
[(1) Atkinson R; J Phys Chem Ref Data Monograph 2 (1994) (2) Atkinson R et al; Atmos Environ 24: 2647-54 (1990) (3) Atkinson R, Carter WPL; Chem Rev 84: 437-70 (1984) (4) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington, DC: Amer Chem Soc pp. 7-4, 7-5 (1990)]**PEER REVIEWED**

Environmental Bioconcentration:

The BCF of **toluene** in eels was reported as 13(1) and the BCF in golden ide was reported as 90(2). According to a classification scheme(3), this BCF data suggests bioconcentration in aquatic organisms is low to moderate.
[(1) Ogata M, Miyake Y; Water Res 12: 1041-4 (1978) (2) Freitag D et al; Chemosphere 14: 1589-1616 (1985) (3) Franke C et al; Chemosphere 29: 1501-14 (1994)]**PEER REVIEWED**

Soil Adsorption/Mobility:

In association with clay minerals, **toluene**'s adsorption is inversely proportional to the pH of the soil. Approximately 40-70% of **toluene** applied to the surface of sandy soils is volatilized.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47 90 (1989)]**PEER REVIEWED**

The Koc of **toluene** was reported as 178 in a sandy soil(1) and as 37 (Wendover silty loam), 160

(Grimsby silt loam), 160 (Vaudreil sandy loam) and 46 (sandy soil)(2). The Koc of **toluene** in lake sediment was measured as 166(3). According to a classification scheme(4), this Koc data suggests that **toluene** is expected to have high to moderate mobility in soil.
[(1) Wilson JT et al; J Environ Qual 10: 501-6 (1981) (2) Nathwani JS, Phillips CR; Chemosphere 6: 157-62 (1977) (3) Kan AT et al; Environ Sci Technol 32: 892-902 (1998) (4) Swann RL et al; Res Rev 85: 17-28 (1983)]**PEER REVIEWED**

Volatilization from Water/Soil:

The Henry's Law constant for **toluene** is 6.64X10-3 atm-cu m/mole(1). This Henry's Law constant indicates that **toluene** is expected to volatilize rapidly from water surfaces(2). Based on this Henry's Law constant, the volatilization half-life from a model river (1 m deep, flowing 1 m/sec, wind velocity of 3 m/sec)(2) is estimated as 1 hour(SRC). The volatilization half-life from a model lake (1 m deep, flowing 0.05 m/sec, wind velocity of 0.5 m/sec)(2) is estimated as 4 days(SRC). **Toluene**'s Henry's Law constant(1) indicates that volatilization from moist soil surfaces may occur(SRC). **Toluene** may volatilize from dry soil surfaces based upon a vapor pressure of 28.4 mm Hg at 25 deg C(3).
[(1) Mackay D et al; Environ Sci Technol 13: 333-36 (1979) (2) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington, DC: Amer Chem Soc pp. 15-1 to 15-29 (1990) (3) Daubert TE, Danner RP; Physical and Thermodynamic Properties of Pure Chemicals Data Compilation Washington, DC: Taylor and Francis (1989)]**PEER REVIEWED**

Environmental Water Concentrations:

Toluene is detected in 28% of National Priority List (NPL) sites in groundwater. Average concentration: 5.18 ppm; Maximum concentration: 1100 ppm. /From table/
[Sullivan, J.B. Jr., G.R. Krieger (eds.). Hazardous Materials Toxicology-Clinical Principles of Environmental Health. Baltimore, MD: Williams and Wilkins, 1992. 304]**PEER REVIEWED**

GROUNDWATER: **Toluene** was detected in groundwater near contaminated wells from gasoline storage tanks at concns of 0.55-6400 ppb(1,2) and groundwater underlying 2 rapid infiltration sites at 0.2 ppb(3). Groundwater under a gasification site 15 months after gasification contained **toluene** at 170-740 ppb(4). In a cluster well study under an old industrial site, mean levels of **toluene** in bedrock wells were 90 ppb while shallow and deep glacial wells were 10 ppb(5). **Toluene** was detected in 1.3% of the samples in the US Ground Water Supply Survey, 1982, at a max concn of 2.9 ppb and a median concn of 0.8 ppb(6).
[(1) Burmaster DE; Environ 24: 6-13, 33-6 (1982) (2) Tester DJ, Harker RJ; Water Pollut Control 80: 614-31 (1981) (3) Hutchins SR et al; Environ Toxicol Chem 2: 195-216 (1983) (4) Stuermer DH et al; Environ Sci Technol 16: 582-7 (1982) (5) Rich CA; Stud Environ Sci 17(Qual Groundwater): 309-14 (1981) (6) Coturvo JA; Sci Total Environ 47: 7-26 (1985)]**PEER REVIEWED**

DRINKING WATER: **Toluene** was detected in 33% of the samples from 30 Canadian treatment facilities at an avg concn of 2 ppb (14 ppb max) in summer months and in 53% of the samples at an avg

concn of <1 ppb (13 ppb max), during winter(1). **Toluene** was detected at concns of 0-2 ppb in drinking water of cities supplied by the Great Lakes(2). **Toluene** was detected in 14% of the samples of drinking water in the US at concns of less than 1 part per trillion(3). In a federal survey of finished drinking water from groundwater sources **toluene** was detected in less than 5% of the samples(4). **Toluene** was detected in 3 New Orleans area water supplies at 0-10 ppb(5). **Toluene** was identified, not quantified, in 60% of drinking water tested in the National Organics Reconnaissance Survey(6). The max concn of **toluene** in tapwater derived from bank-filtered Rhine River water was 1 ppb(7). **Toluene** was detected in 3 contaminated drinking water wells in New Jersey at 55, 260, 6400 ppb whereas the highest concn in drinking water from surface water sources was 6.1 ppb(8). Drinking water supplied from groundwater in England 210 m from a gasoline storage tank contained 0.15 ppb of **toluene**(9). In a 5-city survey in which the water supplies came from different types of sources with various sources of pollution, 2 contained **toluene**, one 0.1 ppb and the other 0.7 ppb(10). **Toluene** was detected in 20 of 182 bottled water samples at an avg concn of 6.92 ug/kg and a range of 0.5-63 ug/kg(11).
[(1) Otson R et al; J Assoc Off Analyt Chem 65: 1370-4 (1982) (2) Williams DT et al; Chemosphere 11: 263-76 (1982) (3) NAS; The Alkyl Benzene USEPA Contract No. 68-02-4655 (1980) (4) Dyksen JE, Hess AF III: J Amer Water Works Assoc 74: 394-403 (1982) (5) Keith LH et al; pp. 329-73 in Identification and analysis of organic pollutants in Water, Keith LH, ed, Ann Arbor Sci Publ (1976) (6) Bedding ND et al; Sci Total Environ 25: 143-67 (1982) (7) Piet GJ, Morra CF; pp. 31-42 in Artificial Groundwater Recharge (Water Res Eng Ser) Huisman L, Olsthorn TN, eds, Pitman Publ (1983) (8) Burmaster DE; Environ 24: 6-13, 33-6 (1982) (9) Tester DJ, Harker RJ; Water Pollut Control 80: 614-31 (1981) (10) Coleman WE et al; pp. 305-27 in Analysis and identification of organic substances in water. Keith L, ed, Ann Arbor, MI: Ann Arbor Sci (1976) (11) Page RD et al; J AOAC Int 76: 26-31 (1993)]**PEER REVIEWED**

SURFACE WATER: **Toluene** was detected in 31 of 204 sites at concns of 1-5 ppb in 14 heavily industrialized river basins in the US(1). **Toluene** was identified, not quantified, in various rivers(2-5). **Toluene** was detected in the Gulf of Mexico at 3-376 parts per trillion(6,7) and the Vineland Sound, MA at 10-54 parts per trillion(8). **Toluene** was detected in the Elbe River, Germany at concns of 30-243 ng/l(9).
[(1) Ewing BB et al; Monitoring to detect previously unrecognized pollutants in surface waters USEPA 560/6-77-015 (appendix USEPA 560/6-77-015a) (1977) (2) Sheldon LS, Hites RA; Environ Sci Technol 12: 1188-94 (1978) (3) Goodley PC, Gordon M; KY Acad Sci 37: 11-5 (1976) (4) Zuercher F, Giger W; Vom Wasser 47: 37-55 (1976) (5) Zou H et al; Wat Res 30: 2003-2008 (1996) (6) Sauer TC Jr; Org Geochem 3: 91-101 (1981) (7) Sauer TC Jr et al; Mar Chem 7: 1-16 (1978) (8) Gschwend PM et al; Environ Sci Technol 16: 31-8 (1982) (9) Gotz R et al; Chemosphere 36: 2103-18 (1998)]**PEER REVIEWED**

RAIN WATER: **Toluene** was detected in rain in west Los Angeles at 76 parts per trillion(1). **Toluene** was detected in 71.4% of the rain samples from 7 rain events in Portland, OR, Feb-Apr 1984, at concns of 40-220 parts per trillion(2).

[(1) Kawamura K, Kaplan IR; Environ Sci Technol 17: 497-501 (1983) (2) Ligocki MP et al; Atmos Environ 19: 1609-17 (1985)]**PEER REVIEWED**

Effluent Concentrations:

Industries in which the mean effluent levels exceed 1000 ppb are: auto and other laundries, iron and steel manufacturing, gum and wood chemicals, pharmaceuticals, organic chemicals/plastics manufacturing, paint and ink formulation. The highest mean value is 52 ppm for pharmaceuticals and the highest maximum values are 230 and 260 ppm for pharmaceuticals and organic chemicals/plastics manufacturing(1). **Toluene** was detected in a plume from General Motors Paint Plant, Janesville, WI at 156 ppb(2). Auto exhaust contained **toluene** at concns of 196-718 mg/cu m(3).
[(1) USEPA; Treatability Manual p. I.9.10-1 to I.9.10-5 USEPA 600/2-82-001a (1981) (2) Sexton K, Westberg H; Environ Sci Technol 14: 329-32 (1980) (3) Tsani-Bazaca E et al; Environ Technol Lett 2: 303-16 (1981)]**PEER REVIEWED**

Toluene was detected in landfill gas emissions at concns of 20,400 ppb, 34,907 ppb and 76,700 ppb(1). **Toluene** was detected in the gas emissions of 7 waste disposal sites in the UK at concns of 10-287 mg/cu m(2). **Toluene** was identified, not quantified, in the exhaust of a moped(3) and 4-stroke lawn mower(4). **Toluene** was detected in car exhaust under normal operating conditions at concns of 3.31-4.52 ppm and an avg of 3.83 ppm(5). The mean emission rate of **toluene** is 89-453 mg/km, with the lowest emission rates occurring at higher driving speeds(5). **Toluene** was detected in the effluent of a hazardous waste incinerator in Germany at a concn of 34 ug/cu m(6).
[(1) Brosseau J, Heitz M; Atmos Environ 28: 285-93 (1994) (2) Allen MR et al; Environ Sci Technol 31: 1054-61 (1997) (3) Ostermark U, Petersson G: Chemosphere 27: 1719-28 (1993) (4) Gabele P; J air Waste Manage Assoc 47: 945-52 (1997) (5) Baily JC et al; Atmos Environ 24A: 43-52 (1990) (6) Jay K, Stiegltz L; Chemosphere 30: 1249-60 (1995)]**PEER REVIEWED**

Sediment/Soil Concentrations:

SEDIMENT: **Toluene** was identified, not quantified in sediment from rivers near industrial facilities in the US(1,2). USEPA STORET DATABASE: **Toluene** was detected in 67 of 397 sediment samples at a median concn of 5.0 ppb dry weight(3). **Toluene** was detected in 33% of the sediment samples from Lake Pontchartrain, LA at an avg concn of 0.7 ppb wet weight(4). **Toluene** was detected at concns of less than 0.1 ng/g to 1.2 ng/g in sediment from rivers near Niigata, Japan(5). **Toluene** was detected in sediment of the Passaic River, NJ at concns of 3-250 ug/kg(6).
[(1) Goodley PC, Gordon M; KY Acad Sci 37: 11-5 (1976) (2) Steinheimer TR et al; Anal Chim Acta 129: 57-67 (1981) (3) Staples CA et al; Environ Toxicol Chem 4: 131-42 (1985) (4) Ferrario JB et al; Bull Environ Contam Toxicol 34: 246-55 (1985) (5) Kawata K et al; Bull Environ Contam Toxicol 58: 893-900 (1997) (6) Iannuzzi TJ et al; Chemosphere 34: 213-31 (1997)]**PEER REVIEWED**

Atmospheric Concentrations:

URBAN/SUBURBAN: In a survey of 3,195 samples obtained from urban areas in the US, **toluene** was

detected at concns of 0-85 ppb (11 ppb median)(1). Average **toluene** concns in US cities range from 0.8-37 ppb with max values ranging from 6.5-1,110 ppb(2-9). Daily variations in concentrations and ratios of **toluene** to benzene indicate that auto traffic is the most common source of atmospheric **toluene**(10,11,12). **Toluene** was detected in Middelsbrough, UK and London, UK at 1.55 and 7.475 ppb, respectively(13). The avg concn of **toluene** inside buses and cars in Taipei, Taiwan was reported as 367 and 599 ug/cu m(14). **Toluene** was detected in various streets in Europe at concns of 87-127 ug/cu m(15). The concn of **toluene** inside automobiles in Paris, France was 178-258 ug/cu m(16).
[(1) Brodzinsky R, Singh HB; Volatile Organics in the Atmosphere: An Assessment of Available Data. p 126-7 SRI contract 68-02-3459 (1982) (2) Singh HB et al; Atmospheric measurements of Selected Hazardous Organic Chemicals USEPA 600/53-81-032 (1981) (3) Altshuller AP et al; Environ Sci Technol 5: 1009-16 (1971) (4) Singh HB et al; Atmos Environ 15: 601-12 (1981) (5) Arnts RR, Meeks SA; Biogenic hydrocarbon contribution to the ambient air of selected areas 128 USEPA 600/3-80-023 (1980) (6) Bozzelli JW et al; Analysis of selected toxic and carcinogenic substances in ambient air in New Jersey, NJ Dept Environ Protect (1980) (7) Lonneman WA et al; Hydrocarbons in Houston air. USEPA 600/3-79-018 pp. 44 (1979) (8) Lioy PJ et al; J Water Pollut Control Fed 33: 649-57 (1983) (9) Pilar S, Graydon WF; Environ Sci Technol 7: 628-71 (1973) (10) Termonia M; Comm Eur Comm EUR 7624 pp. 356-61 (1982) (11) Sexton K, Westberg H; Environ Sci Technol 14: 329-32 (1980) (12) Tsani-Bazaca E et al; Chemosphere 11: 11-23 (1982) (13) Derwent RG; pp. 1-15 in Volatile Organic Compounds in the Atmosphere. Hester RE, Harrison RM, Iss Environ Sci Technol No 4, the Royal Society of Chemistry, Cambridge, UK (1995) (14) Chan CC et al; Atmos Environ 28: 2351-59 (1994) (15) Coursimault A et al; Sci Total Environ 169: 17-23 (1995) (16) Dor F et al; J Air Waste Manage Assoc 45: 103-110 (1995)]**PEER REVIEWED**

INDOOR AIR: **Toluene** was detected at mean concns of 4.8 ug/cu m in telephone communications offices, 10.1 ug/cu m in data center offices and 5.7 ug/cu m in administrative offices in the US(1). **Toluene** was detected in the volatile emissions of newly installed carpet cushions at an emission rate of 4-79 ug/sq m-hr during the first 6 hours after installation(2). **Toluene** was detected in hairdresser salons in Norway at concns of 0.04-0.11 mg/cu m(3).
[(1) Shields HC et al; Indoor air 6: 2-17 (1996) (2) Schaeffer VH et al; J Air Waste Manage Assoc 46: 813-20 (1996) (3) Hollund BE, Moen BE; Ann Occup Hyg 42: 277-81 (1998)]**PEER REVIEWED**

RURAL/REMOTE: **Toluene** was detected in the atmosphere of 115 remote samples taken in the US at concns of 0.057-30 ppb, (0.66 ppb median)(1). **Toluene** was identified, not quantified, in a forest in Germany(2). **Toluene** was detected in Langenbrugge, Germany and West Beckham, UK at concns of 0.441 and 0.999 ppb, respectively(3). **Toluene** was detected at a concn of 0.04 ppb in Izana, Canaries(3)
[(1) Brodzinsky R, Singh HB; Volatile Organics in the Atmosphere: An Assessment of Available Data. pp. 126-7 SRI contract 68-02-3459 (1982) (2) Helmig D et al; Chemosphere 19: 1399-1412 (1989) (3) Derwent RG; pp. 1-15 in Volatile Organic Compounds in the Atmosphere, Hester RE,

Harrison RM. Iss Environ Sci Technol No 4, the Royal Society of Chemistry, Cambridge, UK (1995)]**PEER REVIEWED**

SOURCE DOMINATED: In a survey of 188 source dominated samples from the US, **toluene** was detected at concns of 0.037-5,500 ppb (4.6 ppb median)(1). **Toluene** was detected in the air of the Lipari and BFI landfills in NJ at 0.40 and 310 ppb(2). **Toluene** was detected at concns of 14-22 ppb 4 miles downwind from a General Motors paint plant(3). The avg concn of **toluene** around gasoline pumps during fueling was in the range of 0.14-1.2 mg/cu m and the fenceline concns at the filling stations were in the range of 0.005-0.02 ppm(4). **Toluene** was detected in the Fort McHenry Tunnel, MD at concns of 79-90 ppb(5).
[(1) Brodzinsky R, Singh HB; Volatile Organics in the Atmosphere: An Assessment of Available Data. pp. 126-7 SRI contract 68-02-3459 (1982) (2) Bozzelli JW et al; Analysis of selected toxic and carcinogenic substances in ambient air in New Jersey, NJ Dept Environ Protect (1980) (3) Tsani-Bazaca E et al; Chemosphere 11: 11-23 (1982) (4) American Petroleum Inst; Gasoline Vapor Exposure Assessment at Service Stations. American Petroleum Inst Washington, DC: API Publ 4553 (1993) (5) Zielinska B et al; Atmos Environ 12: 2269-86 (1996)]**PEER REVIEWED**

Food Survey Values:

Toluene was identified, not quantified, in baked potatoes(1), mountain cheese(2), fried bacon(3), fried chicken(4), peanut oil(5) and raw beef(6).
[(1) Coleman EC et al; J Agric Food Chem 29: 42-8 (1981) (2) Dumont JP, Adda J; J Agric Food Chem 26: 364-7 (1978) (3) Ho CT et al; J Agric Food Chem 31: 336-42 (1983) (4) Tang JT et al; J Agric Food Chem 31: 1287-92 (1983) (5) Chung TY et al; J Agric Food Chem 41: 1467-70 (1993) (6) King MF et al; J Agric Food Chem 41: 1974-81 (1993)]**PEER REVIEWED**

Plant Concentrations:

Toluene was identified, not quantified, in the Korean Chamachwi plant(1).
[(1) Chung TY et al; J Agric Food Chem 41: 1693-97 (1993)]**PEER REVIEWED**

Fish/Seafood Concentrations:

Flesh of fish from petroleum contaminated harbor in Japan contained **toluene** at 5 ppm(1). **Toluene** was detected in oysters from Lake Pontchartrain, LA at an avg concn of 3.4 ppb and clams at concns of 18 and 11 ppb(2). **Toluene** was identified, not quantified, in boiled shrimp and crab(3).
[(1) USEPA; Ambient Water Quality Criteria for Toluene. pp. C-1 to C-7 (1980) (2) Ferrario JB et al; Bull Environ Contam Toxicol 34: 246-55 (1985) (3) Misharina TA, Golovnya RV; J High Resol Chromat 15: 332-34 (1992)]**PEER REVIEWED**

Milk Concentrations:

Toluene was identified, not quantified, in 8 samples of mothers' milk from 4 urban areas(1).
[(1) Pellizzari ED et al; Bull Environ Contam Toxicol 28: 322-8 (1982)]**PEER REVIEWED**

Other Environmental Concentrations:

Light oil from coal 12-20% **toluene**; crude oil 1.2-2.4% auto fuel 8-12%(1).
[(1) Walker P; Air Pollution Assessment of Toluene. p. 1-22, 46-92 MTR-7215 Mitre Corp, McLean VA (1976)]**PEER REVIEWED**

Evaporation from gasoline tank: 0.3 - 0.9 vol % of total evaporated hydrocarbons; evaporation from carburetor: 0.5 - 2.4 vol % of total evaporated hydrocarbons.
[Verschueren, K. Handbook of Environmental Data on Organic Chemicals. 3rd ed. New York, NY: Van Nostrand Reinhold Co., 1996. 1723]**PEER REVIEWED**

In exhaust of gasoline engines: 3-8 vol% of total exhaust hydrocarbons; in exhaust of diesel engine: 3% of emitted hydrocarbons; in exhaust of rotary gasoline engine: 16% of emitted hydrocarbons; in exhaust of gasoline engine: 0.1-7.0 ppm (partly crotonaldehyde); in 4 municipal landfill gases in S. Finland (1989-1990): avg 0.23-137, max 143 mg/cu m.
[Verschueren, K. Handbook of Environmental Data on Organic Chemicals. 3rd ed. New York, NY: Van Nostrand Reinhold Co., 1996. 1723]**PEER REVIEWED**

Environmental Standards & Regulations:

FIFRA Requirements:

Toluene is exempted from the requirement of a tolerance when used as a solvent or cosolvent in accordance with good agricultural practice as inert (or occasionally active) ingredients in pesticide formulations applied to growing crops only.
[40 CFR 180.1001(d) (7/1/99)]**PEER REVIEWED**

TSCA Requirements:

Pursuant to section 8(d) of TSCA, EPA promulgated a model Health and Safety Data Reporting Rule. The section 8(d) model rule requires manufacturers, importers, and processors of listed chemical substances and mixtures to submit to EPA copies and lists of unpublished health and safety studies. **Toluene** is included on this list.
[40 CFR 716.120 (7/1/99)]**PEER REVIEWED**

CERCLA Reportable Quantities:

Persons in charge of vessels or facilities are required to notify the National Response Center (NRC) immediately, when there is a release of this designated hazardous substance, in an amount equal to or greater than its reportable quantity of 1000 lb or 454 kg. The toll free number of the NRC is (800) 424-8802; In the Washington D.C. metropolitan area (202) 426-2675. The rule for determining when notification is required is stated in 40 CFR 302.4 (section IV. D.3.b).
[40 CFR 302.4 (7/1/99)]**PEER REVIEWED**

RCRA Requirements:

U220; As stipulated in 40 CFR 261.33, when **toluene**, as a commercial chemical product or manufacturing chemical intermediate or an off-specification commercial chemical product or a manufacturing chemical intermediate, becomes a waste, it must be managed according to Federal and/or State hazardous waste regulations. Also defined as a hazardous waste is any residue, contaminated soil, water, or other debris resulting from the cleanup of a spill, into water or on dry land, of this waste. Generators of small quantities of this waste may qualify for partial exclusion from hazardous waste regulations (40 CFR 261.5).
[40 CFR 261.33 (7/1/99)]**PEER REVIEWED**

F005; When **toluene** is a spent solvent, it is classified as a hazardous waste from a nonspecific source (F005), as stated in 40 CFR 261.31, and must be managed according to State and/or Federal hazardous waste regulations.
[40 CFR 261.31 (7/1/99)]**PEER REVIEWED**

Atmospheric Standards:

This action promulgates standards of performance for equipment leaks of Volatile Organic Compounds (VOC) in the Synthetic Organic Chemical Manufacturing Industry (SOCMI). The intended effect of these standards is to require all newly constructed, modified, and reconstructed SOCMI process units to use the best demonstrated system of continuous emission reduction for equipment leaks of VOC, considering costs, non air quality health and environmental impact and energy requirements. **Toluene** is produced, as an intermediate or a final product, by process units covered under this subpart.
[40 CFR 60.489 (7/1/99)]**PEER REVIEWED**

Listed as a hazardous air pollutant (HAP) generally known or suspected to cause serious health problems. The Clean Air Act, as amended in 1990, directs EPA to set standards requiring major sources to sharply reduce routine emissions of toxic pollutants. EPA is required to establish and phase in specific performance based standards for all air emission sources that emit one or more of the listed pollutants. **Toluene** is included on this list.
[Clean Air Act as amended in 1990, Sect. 112 (b) (1) Public Law 101-549 Nov. 15, 1990]**PEER REVIEWED**

Clean Water Act Requirements:

Toxic pollutant designated pursuant to section 307(a)(1) of the Federal Water Pollution Control Act and is subject to effluent limitations.
[40 CFR 401.15 (7/1/99)] **QC REVIEWED**

Toluene is designated as a hazardous substance under section 311(b)(2)(A) of the Federal Water Pollution Control Act and further regulated by the Clean Water Act Amendments of 1977 and 1978. These regulations apply to discharges of this substance. This designation includes any isomers and hydrates, as well as any solutions and mixtures containing this substance.
[40 CFR 116.4 (7/1/99)] **QC REVIEWED**

For the protection of human health from the toxic properties of **toluene** ... the ambient water criterion is determined to be 14.3 mg/l.
[USEPA; Quality Criteria for Water 1986: Toluene (1986) EPA

440/5-86-001] **QC REVIEWED**

The maximum contaminant level (MCL) set forth by the National Revised Primary Drinking Water Regulations for the organic contaminant **toluene** in community and non-transient, non-community water systems is 1 mg/l.
[40 CFR 141.61 (7/1/99)] **QC REVIEWED**

Federal Drinking Water Standards:

EPA 1000 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

Federal Drinking Water Guidelines:

EPA 1000 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

State Drinking Water Standards:

(CA) CALIFORNIA 150 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

(WI) WISCONSIN 1000 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

State Drinking Water Guidelines:

(AZ) ARIZONA 2000 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

(CT) CONNECTICUT 1000 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

(FL) FLORIDA 40 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

(ME) MAINE 1400 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

(MN) MINNESOTA 1000 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

(WA) WASHINGTON 800 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

(WI) WISCONSIN 343 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

FDA Requirements:

Toluene is an indirect food additive for use only as a component of adhesives.
[21 CFR 175.105 (4/1/99)]**PEER REVIEWED**

Allowable Tolerances:

Toluene is exempted from the requirement of a tolerance when used as a solvent or cosolvent in accordance with good agricultural practice as inert (or occasionally active) ingredients in pesticide formulations applied to growing crops only.
[40 CFR 180.1001(d) (7/1/99)]**PEER REVIEWED**

Chemical/Physical Properties:

Molecular Formula:

C7-H8
PEER REVIEWED

Molecular Weight:

92.14
[Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 79th ed. Boca Raton, FL: CRC Press Inc., 1998-1999.,p. 3-55]**PEER REVIEWED**

Color/Form:

Colorless liquid.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing

Office, 1997. 310]**PEER REVIEWED**

Odor:

Sweet, pungent, benezene-like odor.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 310]**PEER REVIEWED**

Boiling Point:

110.6 deg C
[Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 79th ed. Boca Raton, FL: CRC Press Inc., 1998-1999.,p. 3-55]**PEER REVIEWED**

Melting Point:

-94.9 deg C
[Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 79th ed. Boca Raton, FL: CRC Press Inc., 1998-1999.,p. 3-55]**PEER REVIEWED**

Corrosivity:

Noncorrosive liquid.
[USEPA; Ambient Water Quality Doc: Toluene p.A-1 (1980) EPA 440/5-80-075)]**PEER REVIEWED**

Critical Temperature & Pressure:

Critical temperature: 591.75 K; Critical pressure: 4.108 MPa
[Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 79th ed. Boca Raton, FL: CRC Press Inc., 1998-1999.,p. 6-54]**PEER REVIEWED**

Density/Specific Gravity:

0.8636 @ 20 deg C/4 deg C
[Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 79th ed. Boca Raton, FL: CRC Press Inc., 1998-1999.,p. 3-55]**PEER REVIEWED**

Heat of Combustion:

3910.3 KJ/mol
[Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 79th ed. Boca Raton, FL: CRC Press Inc., 1998-1999.,p. 6-111]**PEER REVIEWED**

Heat of Vaporization:

38.01 KJ/mol @ 25 deg C
[Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 79th ed. Boca Raton, FL: CRC Press Inc., 1998-1999.,p. 6-111]**PEER REVIEWED**

Octanol/Water Partition Coefficient:

log Kow= 2.73
[Hansch, C., Leo, A., D. Hoekman. Exploring QSAR - Hydrophobic, Electronic, and Steric Constants. Washington, DC: American Chemical Society., 1995. 31]**PEER REVIEWED**

Solubilities:

Miscible with alcohol, chloroform, ether, acetone, glacial acetic acid, carbon disulfide
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 1626]**PEER REVIEWED**

Soluble in ethanol, benzene, diethyl ether, acetone, chloroform, glacial acetic acid and carbon disulfide; insoluble in water.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47 79 (1989)]**PEER REVIEWED**

In water, 526 mg/l @ 25 deg C
[Sanemasa I et al; Bull Chem Soc Japan 55: 1054-62 (1982)]**PEER REVIEWED**

Spectral Properties:

SADTLER REF NUMBER: 419 (IR, PRISM); 119 (IR, GRATING); MAX ABSORPTION (ALCOHOL): 207 NM (LOG E= 3.97); 260 NM LOG E= 2.48)
[Weast, R.C. (ed.). Handbook of Chemistry and Physics. 60th ed. Boca Raton, Florida: CRC Press Inc., 1979.,p. C-518]**PEER REVIEWED**

Index of refraction: 1.4967 @ 20 deg C/D
[Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 79th ed. Boca Raton, FL: CRC Press Inc., 1998-1999.,p. 3-55]**PEER REVIEWED**

IR: 3574 (Coblentz Society Spectral Collection)
[Weast, R.C. and M.J. Astle. CRC Handbook of Data on Organic Compounds. Volumes I and II. Boca Raton, FL: CRC Press Inc. 1985.,p. V2 360]**PEER REVIEWED**

UV: 155 (Sadtler Research Laboratories Spectral Collection)
[Weast, R.C. and M.J. Astle. CRC Handbook of Data on Organic Compounds. Volumes I and II. Boca Raton, FL: CRC Press Inc. 1985.,p. V2 360]**PEER REVIEWED**

NMR: 157 (Varian Associates NMR Spectra Catalogue)
[Weast, R.C. and M.J. Astle. CRC Handbook of Data on Organic Compounds. Volumes I and II. Boca Raton, FL: CRC Press Inc. 1985.,p. V2 360]**PEER REVIEWED**

MASS: 189 (Atlas of Mass Spectral Data, John Wiley & Sons, New York)
[Weast, R.C. and M.J. Astle. CRC Handbook of Data on Organic Compounds. Volumes I and II. Boca Raton, FL: CRC Press Inc. 1985.,p. V2 360]**PEER REVIEWED**

Intense mass spectral peaks: 65 m/z, 91 m/z, 92 m/z
[Pfleger, K., H. Maurer and A. Weber. Mass Spectral and GC Data of Drugs, Poisons and their Metabolites. Parts I and II. Mass Spectra Indexes. Weinheim, FederalRepublic of Germany. 1985. 104]**PEER REVIEWED**

Surface Tension:

29.71 dyne/cm @ 10 deg C; 28.93 dyne/cm @ 20 deg C; 24.96 dyne/cm @ 50 deg C; 21.98 dyne/cm @ 75 deg C; 19.01 dyne/cm @ 100 deg C
[Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 79th ed. Boca Raton, FL: CRC Press Inc., 1998-1999.,p. 6-137]**PEER REVIEWED**

Vapor Density:

3.1 (Air=1)
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994.,p. 1304-5]**PEER REVIEWED**

Vapor Pressure:

28.4 mm Hg @ 25 deg C
[Daubert, T.E., R.P. Danner. Physical and Thermodynamic Properties of Pure Chemicals Data Compilation. Washington, D.C.: Taylor and Francis, 1989.]**PEER REVIEWED**

Viscosity:

0.778 cP @ 0 deg C; 0.560 cP @ 25 deg C; 0.424 cP @ 50 deg C; 0.333 cP @ 75 deg C; 0.270 cP @ 100 deg C
[Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 79th ed. Boca Raton, FL: CRC Press Inc., 1998-1999.,p. 6-173]**PEER REVIEWED**

Other Chemical/Physical Properties:

CONVERSION FACTORS: 1 PPM= 3.76/CU M; 1 MG/L= 226 PPM.
[Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965. 66]**PEER REVIEWED**

Ratio of Specific Heats of Vapor (Gas): 1.089; floats on water
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Partition coefficients at 37 deg C for **toluene** into blood= 15.6; into oil= 1,470.
[Sato A, Nakajima T; Scand J Work Environ Health 13: 81-93 (1987)]**PEER REVIEWED**

Henry's Law constant = 6.64X10-3 atm-cu m/mole @ 25 deg C
[Mackay D et al; Environ Sci Technol 13: 333-6 (1979)]**PEER REVIEWED**

Hydroxyl radical rate constant = 5.96X10-12 cu cm/molecule-sec @ 25 deg C
[Atkinson R; J Phys Chem Ref Data Monograph No. 2 (1994)]**PEER REVIEWED**

Chemical Safety & Handling:

DOT Emergency Guidelines:

Fire or explosion: Highly flammable: Will be easily ignited by heat, sparks or flames. Vapors may form explosive mixtures with air. Vapors may travel to source of ignition and flash back. Most vapors are heavier than air. They will spread along ground and collect in low or confined areas (sewers, basements, tanks). Vapor explosion hazard indoors, outdoors or in sewers. Some may polymerize (P) explosively when heated or involved in a fire. Runoff to sewer may create fire or explosion hazard. Containers may explode when heated. Many liquids are lighter than water.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-130]**PEER REVIEWED**

Health: May cause toxic effects if inhaled or absorbed through skin. Inhalation or contact with material may irritate or burn skin and eyes. Fire will produce irritating, corrosive and/or toxic gases. Vapors may cause dizziness or suffocation. Runoff from fire control or dilution water may cause pollution.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-130]**PEER REVIEWED**

Public safety: Call Emergency Response Telephone Numbers. ... Isolate spill or leak area immediately for at least 50 to 100 meters (160 to 330 feet) in all directions. Keep unauthorized personnel away. Stay upwind. Keep out of low areas. Ventilate closed spaces before entering.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training

(DHM-50), Washington, D.C. (1996).,p. G-130]**PEER REVIEWED**

Protective clothing: Wear positive pressure self-contained breathing apparatus (SCBA). Structural firefighters' protective clothing will only provide limited protection.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-130]**PEER REVIEWED**

Evacuation: Large spill: Consider initial downwind evacuation for at least 300 meters (1000 feet). Fire: If tank, rail car or tank truck is involved in a fire, isolate for 800 meters (1/2 mile) in all directions; also, consider initial evacuation for 800 meters (1/2 mile) in all directions.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-130]**PEER REVIEWED**

Fire: Caution: All these products have a very low flash point: Use of water spray when fighting fire may be inefficient. Small fires: Dry chemical, CO2, water spray or regular foam. Large fires: Water spray, fog or regular foam. Do not use straight streams. Move containers from fire area if you can do it without risk. Fire involving tanks or car/trailer loads: Fight fire from maximum distance or use unmanned hose holders or monitor nozzles. Cool containers with flooding quantities of water until well after fire is out. Withdraw immediately in case of rising sound from venting safety devices or discoloration of tank. Always stay away from the ends of tanks. For massive fire, use unmanned hose holders or monitor nozzles; if this is impossible, withdraw from area and let fire burn.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-130]**PEER REVIEWED**

Spill or leak: Eliminate all ignition sources (no smoking, flares, sparks or flames in immediate area). All equipment used when handling the product must be grounded. Do not touch or walk through spilled material. Stop leak if you can do it without risk. Prevent entry into waterways, sewers, basements or confined areas. A vapor suppressing foam may be used to reduce vapors. Absorb or cover with dry earth, sand or other non-combustible material and transfer to containers. Use clean non-sparking tools to collect absorbed material. Large spills: Dike far ahead of liquid spill for later disposal. Water spray may reduce vapor; but may not prevent ignition in closed spaces.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs

Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-130]**PEER REVIEWED**

First aid: Move victim to fresh air. Call emergency medical care. Apply artificial respiration if victim is not breathing. Administer oxygen if breathing is difficult. Remove and isolate contaminated clothing and shoes. In case of contact with substance, immediately flush skin or eyes with running water for at least 20 minutes. Wash skin with soap and water. Keep victim warm and quiet. Effects of exposure (inhalation, ingestion or skin contact) to substance may be delayed. Ensure that medical personnel are aware of the material(s) involved, and take precautions to protect themselves.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-130]**PEER REVIEWED**

Odor Threshold:

2.14 ppm (8 mg/cu m). Odor recognition level is reported as 1.03 to 140 ug/cu m.
[Cleland, J.G., G.L. Kingsbury. Multimedia Environmental Goals for Environmental Assessment. Volume 1. EPA-600/7-77-136a. Research Triangle Park, NC: EPA, Nov. 1977.,p. E-146]**PEER REVIEWED**

Odor in air= 1.30x10+11 mol/cu cm
[Fazzalari, F.A. (ed.). Compilation of Odor and Taste Threshold Values Data. ASTM Data Series DS 48A (Committee E-18). Philadelphia, PA: American Society for Testing and Materials, 1978. 158]**PEER REVIEWED**

Skin, Eye and Respiratory Irritations:

A human eye irritant. An experimental skin and severe eye irritant.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 3190]**PEER REVIEWED**

Fire Potential:

Flammable liquid. A very dangerous fire hazard when exposed to heat, flame, or oxidizers.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 3190]**PEER REVIEWED**

NFPA Hazard Classification:

Health: 2. 2= Materials that, on intense or continued (but not chronic) exposure, could cause temporary incapacitation or possible residual injury, including those requiring the use of respiratory protective equipment that has an independent air supply. These materials are hazardous to health, but areas may be entered freely if personnel are provided with full-face mask self-contained breathing apparatus that

provides complete eye protection.
[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 325-87]**PEER REVIEWED**

Flammability: 3. 3= This degree includes Class IB and IC flammable liquids and materials that can be easily ignited under almost all normal temperature conditions. Water may be ineffective in controlling or extinguishing fires in such materials.
[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 325-87]**PEER REVIEWED**

Reactivity: 0. 0= This degree includes materials that are normally stable, even under fire exposure conditions, and that do not react with water. Normal fire fighting procedures may be used.
[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 325-87]**PEER REVIEWED**

Flammable Limits:

Lower flammable limit: 1.1% by volume; Upper flammable limit: 7.1% by volume
[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 325-87]**PEER REVIEWED**

Flash Point:

40 deg F (4 deg C) (Closed cup)
[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 325-87]**PEER REVIEWED**

16 deg C (Open cup)
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Autoignition Temperature:

896 DEG F (480 DEG C)
[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 325-87]**PEER REVIEWED**

Fire Fighting Procedures:

TO FIGHT FIRE, USE FOAM, CO2, DRY CHEMICAL.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 3190]**PEER REVIEWED**

Approach fire from upwind to avoid hazardous vapors and toxic decomposition
[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 49-127]**PEER REVIEWED**

If material on fire or involved in fire: Do not extinguish fire unless flow can be stopped or safely confined. Use water in flooding quantities as fog. Solid streams of water may spread fire. Cool all affected containers with flooding quantities of water. Apply water from as far a distance as possible. Use foam, dry chemical, or carbon dioxide.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 1057]**PEER REVIEWED**

Toxic Combustion Products:

MODERATELY DANGEROUS; WHEN HEATED, EMITS TOXIC FUMES /WHICH/ CAN REACT VIGOROUSLY WITH OXIDIZING MATERIALS.
[Sax, N.I. Dangerous Properties of Industrial Materials. 6th ed. New York, NY: Van Nostrand Reinhold, 1984. 2588]**PEER REVIEWED**

Firefighting Hazards:

Vapor is heavier than air and may travel a considerable distance to a source of ignition and flash back.
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Flame speed equals 37 cm/sec.
[Environment Canada; Tech Info for Problem Spills: Toluene (Draft) p.3 (1979)]**PEER REVIEWED**

Explosive Limits & Potential:

LEL: 1.27%; UEL: 7%.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 3190]**PEER REVIEWED**

Hazardous Reactivities & Incompatibilities:

Frozen bromine trifluoride reacts violently with **toluene** at -80 deg C.
[Bretherick, L. Handbook of Reactive Chemical Hazards. 4th ed. Boston, MA: Butterworth-Heinemann Ltd., 1990 91]**PEER REVIEWED**

A mixture of /dinitrogen/ tetraoxide and **toluene** exploded, possibly initiated by impurities.
[Bretherick, L. Handbook of Reactive Chemical Hazards. 4th ed. Boston, MA: Butterworth-Heinemann Ltd., 1990 1353]**PEER REVIEWED**

Lack of proper control in nitration of **toluene** with mixed acids /nitric/ may lead to runaway or explosive reaction. A contributory factor is the oxidative formation, and subsequent nitration and decomposition of

nitrocresols.
[Bretherick, L. Handbook of Reactive Chemical Hazards. 4th ed. Boston, MA: Butterworth-Heinemann Ltd., 1990 1165]**PEER REVIEWED**

When /tetranitromethane is/ mixed with hydrocarbons in approximately stoichiometric proportions, a sensitive highly explosive mixture is produced which needs careful handling ... . Explosion of only 10 g of a mixture with **toluene** caused 10 deaths and 20 severe injuries. The mixture contained excess **toluene** in error.8
[Bretherick, L. Handbook of Reactive Chemical Hazards. 4th ed. Boston, MA: Butterworth-Heinemann Ltd., 1990 189]**PEER REVIEWED**

Interaction /of uranium hexafluoride/ with ... **toluene** ... is very vigorous, with separation of carbon, and violent with ethanol or water.
[Bretherick, L. Handbook of Reactive Chemical Hazards. 4th ed. Boston, MA: Butterworth-Heinemann Ltd., 1990 1126]**PEER REVIEWED**

Incompatible with strong oxidizers.
[Sittig, M. Handbook of Toxic and Hazardous Chemicals and Carcinogens, 1985. 2nd ed. Park Ridge, NJ: Noyes Data Corporation, 1985. 869]**PEER REVIEWED**

Strong oxidizers.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 310]**PEER REVIEWED**

Reacts photochemically with nitrogen oxides or halogens to form nitrotoluene, nitrobenzene and nitrophenol and halogenated products, respectively.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47 79 (1989)]**PEER REVIEWED**

Explosive reaction with 1,3-dichloro-5,5-dimethyl-2,4-imidazolididione; dinitrogen tetraoxide; concentrated nitric acid, sulfuric acid + nitric acid; N2O4; AgClO4; BrF3; Uranium hexafluoride; sulfur dichloride. Forms an explosive mixture with tetranitromethane.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 3190]**PEER REVIEWED**

Hazardous Decomposition:

When heated to decomposition it emits acrid smoke and irritating fumes.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 3190]**PEER REVIEWED**

Prior History of Accidents:

The wreck of the MV Ariadne, a Panamanian flag container ship, is examined as a case study of a hazardous substance emergency response in a third world country. /The ship/, carrying a cargo of heavy fuel oil, tetraethyl lead, xylene, **toluene**, methyl isobutyl ketone, butyl acetate, ethyl acetate, and acetone was grounded while departing the harbor of Mogadishu, Somalia. The Somalian government requested a team of technical advisors to help respond appropriately to the emergency. The major issues addressed by the advisory team were the need for additional salvage equipment and expertise, the danger of toxic fumes from the fire and explosions aboard the ship, the presence and possible release of tetraethyl lead, possible port blockage by the wreck, recovery of the chemical drums, and the extent of environmental damage caused by the release of oil, pesticides, and tetraethyl lead into the harbor. ...
[Heare SF et al; 1986 Hazard Matl Spill Conf p.12-18 (1986)]**PEER REVIEWED**

Immediately Dangerous to Life or Health:

500 ppm
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 310]**PEER REVIEWED**

Protective Equipment & Clothing:

Protective clothing should include gloves, barrier creams, eye goggles or face shields, and a cartridge-type or self-contained breathing apparatus.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1332]**PEER REVIEWED**

WEAR SELF-CONTAINED BREATHING APPARATUS; WEAR GOGGLES IF EYE PROTECTION NOT PROVIDED.
[National Fire Protection Association. Fire Protection Guide on Hazardous Materials. 9th ed. Boston, MA: National Fire Protection Association, 1986.,p. 49-89]**PEER REVIEWED**

Eye protection: Glasses having shatter-resistant glass or equivalent lenses and side shields to protect the eyes from **toluene** splashes.
[NIOSH; Criteria Document: Toluene p.8 (1973) DHEW Pub. NIOSH 73-11023]**PEER REVIEWED**

If, for the purpose of maintenance or cleaning, a person is required to enter a vessel or similar area which has contained **toluene**, all suitable precautions for work in confined spaces should be adopted. Respiratory protection of the airline or self-contained type is essential; Reliance should not be placed on a canister respirator for such work. Workers whose hands may be exposed to **toluene** should wear suitable gloves or barrier creams. A thick layer of barrier cream should be applied. Under certain circumstances the use of a mask may be necessary for this type of work.
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 2185]**PEER REVIEWED**

Respirator selection: 500 ppm: Chemical cartridge respirator with organic vapor cartridge/supplied-air

respirator/self-contained breathing apparatus; 1000 ppm: Chemical cartridge respirator with organic vapor cartridge with full facepiece; 2000 ppm: Gas mask with organic vapor canister/supplied-air respirator with full facepiece, helmet, or hood/self-contained breathing apparatus with full facepiece; Escape: gas mask with organic vapor canister/self-contained breathing apparatus.
[Sittig, M. Handbook of Toxic and Hazardous Chemicals and Carcinogens, 1985. 2nd ed. Park Ridge, NJ: Noyes Data Corporation, 1985. 870]**PEER REVIEWED**

Wear appropriate personal protective clothing to prevent skin contact.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 310]**PEER REVIEWED**

Wear appropriate eye protection to prevent eye contact.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 310]**PEER REVIEWED**

Recommendations for respirator selection. Max concn for use: 500 ppm. Respirator Class(es): Any chemical cartridge respirator with organic vapor cartridge(s). May require eye protection. Any powered, air-purifying respirator with organic vapor cartridge(s). May require eye protection. Any air-purifying, full-facepiece respirator (gas mask) with a chin-style, front- or back-mounted organic vapor canister. Any supplied-air respirator. May require eye protection. Any self-contained breathing apparatus with a full facepiece.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 310]**PEER REVIEWED**

Recommendations for respirator selection. Condition: Emergency or planned entry into unknown concn or IDLH conditions: Respirator Class(es): Any self-contained breathing apparatus that has a full facepiece and is operated in a pressure-demand or other positive-pressure mode. Any supplied-air respirator that has a full facepiece and is operated in a pressure-demand or other positive-pressure mode in combination with an auxiliary self-contained breathing apparatus operated in pressure-demand or other positive-pressure mode.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 310]**PEER REVIEWED**

Recommendations for respirator selection. Condition: Escape from suddenly occurring respiratory hazards: Respirator Class(es): Any air-purifying, full-facepiece respirator (gas mask) with a chin-style, front- or back-mounted organic vapor canister. Any appropriate escape-type, self-contained breathing apparatus.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 310]**PEER REVIEWED**

Preventive Measures:

Drench-type showers, eye-wash fountains should be installed and maintained to provide prompt, immediate access.
[NIOSH; Criteria Document: Toluene p.9 (1973) DHEW Pub. NIOSH 73-11023]**PEER REVIEWED**

Open lights or other agencies liable to ignite the vapor should be excluded from areas where the liquid is liable to be exposed in use or by accident.
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 2185]**PEER REVIEWED**

A major concern in the painting studio is solvents, /including **toluene**/. ... Precautions include ... use of dilution and local exhaust ventilation, control of storage areas, disposal of solvent soaked rags in covered containers, minimizing skin exposure and the use of respirators and other personal protective equipment. The control of fire hazards is also important, since many of the solvents are highly flammable.
[Hart C; J Environ Health 49 (5): 282-86 (1987)]**PEER REVIEWED**

Contact lenses should not be worn when working with this chemical.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 310]**PEER REVIEWED**

SRP: The scientific literature for the use of contact lenses in industry is conflicting. The benefit or detrimental effects of wearing contact lenses depend not only upon the substance, but also on factors including the form of the substance, characteristics and duration of the exposure, the uses of other eye protection equipment, and the hygiene of the lenses. However, there may be individual substances whose irritating or corrosive properties are such that the wearing of contact lenses would be harmful to the eye. In those specific cases, contact lenses should not be worn. In any event, the usual eye protection equipment should be worn even when contact lenses are in place.
PEER REVIEWED

If material not on fire and not involved in fire: Keep sparks, flames, and other sources of ignition away. Keep material out of water sources and sewers. Build dikes to contain flow as necessary. Attempt to stop leak if without undue personnel hazard. Use water spray to knock-down vapors.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 1057]**PEER REVIEWED**

Personnel protection: Avoid breathing vapors. Keep upwind. ... Do not handle broken packages unless wearing appropriate personal protective equipment. Wash away any material which may have contacted the body with copious amounts of water or soap and water.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 1057]**PEER REVIEWED**

If material leaking (not on fire): Consider evacuation from downwind area based on amount of material spilled, location and weather conditions.
[Association of American Railroads. Emergency Handling of Hazardous

Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 1057]**PEER REVIEWED**

The worker should immediately wash the skin when it becomes contaminated.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 310]**PEER REVIEWED**

Work clothing that becomes wet should be immediately removed due to its flammability hazard.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 310]**PEER REVIEWED**

Shipment Methods and Regulations:

No person may /transport,/ offer or accept a hazardous material for transportation in commerce unless that person is registered in conformance ... and the hazardous material is properly classed, described, packaged, marked, labeled, and in condition for shipment as required or authorized by ... /the hazardous materials regulations (49 CFR 171-177)./
[49 CFR 171.2 (7/1/99)]**PEER REVIEWED**

The International Air Transport Association (IATA) Dangerous Goods Regulations are published by the IATA Dangerous Goods Board pursuant to IATA Resolutions 618 and 619 and constitute a manual of industry carrier regulations to be followed by all IATA Member airlines when transporting hazardous materials.
[IATA. Dangerous Goods Regulations. 40th Ed. Montreal, Canada and Geneva, Switzerland: International Air Transport Association, Dangerous Goods Regulations, 1999. 217]**PEER REVIEWED**

The International Maritime Dangerous Goods Code lays down basic principles for transporting hazardous chemicals. Detailed recommendations for individual substances and a number of recommendations for good practice are included in the classes dealing with such substances. A general index of technical names has also been compiled. This index should always be consulted when attempting to locate the appropriate procedures to be used when shipping any substance or article.
[IMDG; International Maritime Dangerous Goods Code; International Maritime Organization p.3285 (1998)]**PEER REVIEWED**

Storage Conditions:

Outside or detached storage is preferred. Inside storage should be in a standard flammable liquids storage warehouse, room, or cabinet. Separate from oxidizing materials.
[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 49-127]**PEER REVIEWED**

Use ambient storage temperature.
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Cleanup Methods:

Eliminate all ignition sources. Stop or control the leak, if this can be done without undue risk. Use water spray to cool and disperse vapors and protect personnel. Absorb in noncombustible material for proper disposal. Control runoff and isolate discharged material for proper disposal.
[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 49-197]**PEER REVIEWED**

1. REMOVE ALL IGNITION SOURCES. 2. VENTILATE AREA OF SPILL OR LEAK. 3. FOR SMALL QUANTITIES, ABSORB ON PAPER TOWELS. EVAPORATE IN SAFE PLACE (SUCH AS FUME HOOD). ALLOW SUFFICIENT TIME FOR EVAPORATING VAPORS TO COMPLETELY CLEAR HOOD DUCTWORK. BURN PAPER IN SUITABLE LOCATION AWAY FROM COMBUSTIBLE MATERIALS.
[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) PublicationNo. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981. 4]**PEER REVIEWED**

Fluorocarbon water foam may be used to diminish vapors and provide wet down.
[Environment Canada; Tech Info for Problem Spills: Toluene (Draft) p.94 (1982)]**PEER REVIEWED**

Cellosive and hycar absorbent materials, may be used for vapor suppression and/or containment of **toluene**.
[Environment Canada; Tech Info for Problem Spills: Toluene (Draft) p.94 (1982)]**PEER REVIEWED**

Treat contaminated water by gravity separation of solids, followed by skimming of surface. Pass through dual media filtration and carbon adsorption units (carbon ratio 1.0 kg to 10.0 kg soluble material). Return waste water from backwash to gravity separator.
[Environment Canada; Tech Info for Problem Spills: Toluene (Draft) p.94 (1982)]**PEER REVIEWED**

Environmental considerations - Land Spill: Dig a pit, pond, lagoon, holding area to contain liquid or solid material. /SRP: If time permits, pits, ponds, lagoons, soak holes, or holding areas should be sealed with an impermeable flexible membrane liner./ Dike surface flow using soil, sand bags, foamed polyurethane, or foamed concrete. Absorb bulk liquid with fly ash, cement powder,or commercial sorbents. Apply "universal" gelling agent to immobilize spill. Apply appropriate foam to diminish vapor and fire hazard.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 1057]**PEER REVIEWED**

Environmental considerations - Water Spill: Use natural barriers or oil spill control boom to limit spill travel. Use surface active agent (eg Detergent, soaps, alcohols), if approved by EPA. Inject "universal" gelling agent to solidify encircled spill and increase effectiveness of booms. If dissolved, in region of 10 ppm or greater concentration, apply activated carbon at ten times the spilled amount. Remove trapped

material with suction hoses. Use mechanical dredges or lifts to remove immobilized masses of pollutants and precipitates.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 1057]**PEER REVIEWED**

Environmental considerations - Air Spill: Apply water spray or mist to knock down vapors.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 1057]**PEER REVIEWED**

Disposal Methods:

Generators of waste (equal to or greater than 100 kg/mo) containing this contaminant, EPA hazardous waste numbers U220, and F005 must conform with USEPA regulations in storage, transportation, treatment and disposal of waste.
[40 CFR 240-280, 300-306, 702-799 (7/1/90)]**PEER REVIEWED**

Toluene is a waste chemical stream constituent which may be subjected to ultimate disposal by controlled incineration.
[USEPA; Engineering Handbook for Hazardous Waste Incineration p.2-9 (1981) EPA 68-03-3025]**PEER REVIEWED**

A good candidate for liquid injection incineration at a temperature range of 650 to 1,600 deg C and a residence time of 0.1 to 2 seconds. A good candidate for rotary kiln incineration at a temperature range of 820 to 1,600 deg C and residence times of seconds for liquids and gases, and hours for solids. A good candidate for fluidized bed incineration at a temperature range of 450 to 980 deg C and residence times of seconds for liquids and gases, and longer for solids.
[USEPA; Engineering Handbook for Hazardous Waste Incineration p.3-16 (1981) EPA 68-03-3025]**PEER REVIEWED**

Additional flammable solvent may be added to increase incineration efficiency. Following treatment at a spill site or waste management facility, the resultant sludge can be disposed of to a secure landfill.
[Environment Canada; Tech Info for Problem Spills: Toluene (Draft) p.96 (1982)]**PEER REVIEWED**

LARGE QUANTITIES CAN BE RECLAIMED OR COLLECTED & ATOMIZED IN SUITABLE COMBUSTION CHAMBER. **TOLUENE** SHOULD NOT BE ALLOWED TO ENTER A CONFINED SPACE, SUCH AS SEWER, BECAUSE OF POSSIBILITY OF EXPLOSION. ... DISPOSAL METHODS: **TOLUENE** MAY BE DISPOSED OF BY ATOMIZING IN SUITABLE COMBUSTION CHAMBER.
[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) PublicationNo. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981. 4]**PEER REVIEWED**

The following wastewater treatment technologies have been investigated for **toluene**: biological treatment.
[USEPA; Management of Hazardous Waste Leachate, EPA Contract

No.68-03-2766 p.E-48 (1982)]**PEER REVIEWED**

The following wastewater treatment technologies have been investigated for **toluene**: stripping.
[USEPA; Management of Hazardous Waste Leachate, EPA Contract No.68-03-2766 p.E-97 (1982)]**PEER REVIEWED**

The following wastewater treatment technologies have been investigated for **toluene**: solvent extraction.
[USEPA; Management of Hazardous Waste Leachate, EPA Contract No.68-03-2766 p.E-112 (1982)]**PEER REVIEWED**

The following wastewater treatment technologies have been investigated for **toluene**: activated carbon.
[USEPA; Management of Hazardous Waste Leachate, EPA Contract No.68-03-2766 p.E-148 (1982)]**PEER REVIEWED**

Occupational Exposure Standards:

OSHA Standards:

Permissible Exposure Limit: Table Z-2 8-hr Time Weighted Avg: 200 ppm.
[29 CFR 1910.1000 (7/1/99)]**PEER REVIEWED**

Permissible Exposure Limit: Table Z-2 Acceptable Ceiling Concentration: 300 ppm.
[29 CFR 1910.1000 (7/1/99)]**PEER REVIEWED**

Permissible Exposure Limit: Table Z-2 Acceptable maximum peak above the acceptable ceiling concentration for an 8-hour shift. Concentration: 500 ppm. Maximum Duration: 10 minutes.
[29 CFR 1910.1000 (7/1/99)]**PEER REVIEWED**

Vacated 1989 OSHA PEL TWA 100 ppm (375 mg/cu m); STEL 150 ppm (560 mg/cu m) is still enforced in some states.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 372]**PEER REVIEWED**

Threshold Limit Values:

8 Hr Time Weighted Avg (TWA) 50 ppm, skin
[American Conference of Governmental Industrial Hygienists. TLVs and BEIs. Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. Cincinnati, OH. 2000. 67]**QC REVIEWED**

Biological Exposure Index (BEI): Hippuric acid in urine at end of shift is 1.65 g/g creatinine. The determinant is usually present in a significant amt in biological specimens collected from subjects who have not been occupationally exposed. Such background levels are incl in the BEI value. The determinant is nonspecific, since it is observed after exposure to some other chemicals. These nonspecific tests are preferred because they are easy to use and usually offer a better correlation with exposure than specific tests. In such instances, a BEI for a specific, less quantitative biological determinant is recommended as a confirmatory test.
[American Conference of Governmental Industrial Hygienists. TLVs and

BEIs. Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. Cincinnati, OH. 2000. 101]**QC REVIEWED**

Biological Exposure Index (BEI) adoption (1998): **Toluene** in venous blood prior to last shift of workweek is 0.5 mg/l.
[American Conference of Governmental Industrial Hygienists. TLVs and BEIs. Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. Cincinnati, OH. 2000. 101]**QC REVIEWED**

Excursion Limit Recommendation: Excursions in worker exposure levels may exceed three times the TLV-TWA for no more than a total of 30 min during a work day, and under no circumstances should they exceed five times the TLV-TWA, provided that the TLV-TWA is not exceeded.
[American Conference of Governmental Industrial Hygienists. TLVs and BEIs. Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. Cincinnati, OH. 2000. 6]**QC REVIEWED**

Biological Exposure Index (BEI): Determinant: o-Cresol in urine; Sampling Time: end of shift; BEI:0.5 mg/L. The determinant is usually present in a significant amt in biological specimens collected from subjects who have not been occupationally exposed. Such background levels are incl in the BEI value.
[American Conference of Governmental Industrial Hygienists. TLVs and BEIs. Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. Cincinnati, OH. 2000. 101]**QC REVIEWED**

A4. A4= Not classifiable as a human carcinogen.
[American Conference of Governmental Industrial Hygienists. TLVs and BEIs. Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. Cincinnati, OH. 2000. 67]**QC REVIEWED**

NIOSH Recommendations:

Recommended Exposure Limit: 10 Hr Time-Weighted Avg: 100 ppm (375 mg/cu m).
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 310]**PEER REVIEWED**

Recommended Exposure Limit: 15 Min Short-Term Exposure Limit: 150 ppm (560 mg/cu m).
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 310]**PEER REVIEWED**

Immediately Dangerous to Life or Health:

500 ppm
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH)

Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 310]**PEER REVIEWED**

Other Occupational Permissible Levels:

Australia: 100 ppm, STEL 150 ppm (substance under review) (1990); Federal Republic of Germany: 100 ppm, short-term level 500 ppm, 30 min, twice per shift, Pregnancy group B, a risk of damage to the developing embryo or fetus must be considered to be probable (1992); Sweden: 80 ppm, short-term value 100 ppm, 15 min, planning of new plants or alterations of old ones, 50 ppm (1990); United Kingdom: 50 ppm, 10-min STEL 150 ppm, skin (1991).
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Volumes I,II, III. Cincinnati, OH: ACGIH, 1991. 1577]**PEER REVIEWED**

Emergency Response Planning Guidelines (ERPG): ERPG(1) 50 ppm (no more than mild, transient effects) for up to 1 hr exposure; ERPG(2) 300 ppm (without serious, adverse effects) for up to 1 hr exposure; ERPG(3) 1000 ppm (not life threatening) up to 1 hr exposure.
[American Industrial Hygiene Association. The AIHA 1999 Emergency Response Planning Guidelines and Workplace Environmental Exposure Level Guides Handbook.American Industrial Hygiene Association. Fairfax, VA 1999. 27]**PEER REVIEWED**

Manufacturing/Use Information:

Major Uses:

In manufacture benzoic acid, benzaldehyde, explosives, dyes, and many other organic compounds; as a solvent for paints, lacquers, gums, resins, in the extraction of various principles from plants; as gasoline additive.
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 1626]**PEER REVIEWED**

DILUENT FOR PHOTOGRAVURE INKS
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 2184]**PEER REVIEWED**

IN FABRIC & PAPER COATING, MFR ARTIFICIAL LEATHER
[Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965. 67]**PEER REVIEWED**

Used in cements, solvents, spot removers, cosmetics, antifreezes, and inks.
[Gleason MN; Chem Tox of Comm Prod, 3rd Ed, 1969 as cited in USEPA; Health Assessment Document: Toluene (Draft) (1982) EPA-600/8-82-008]**PEER REVIEWED**

Asphalt and naphtha constituent. Detergent manufacture.

[USEPA. Identification of Organic Cmpds in Effluents from Industrial Sources, (1975) EPA 560/3-75-002]**PEER REVIEWED**

Mfg benzene derivatives, caprolactam, saccharin, medicines, dyes, perfumes, TNT; solvent recovery plants; component of gasoline; solvent for paints and coatings, gums, resins, rubber and vinyl organosol; diluent and thinner in nitrocellulose lacquers; adhesive solvent in plastic toys and model airplanes; detergent mfg; gasoline and naphtha constituent.
[Verschueren, K. Handbook of Environmental Data on Organic Chemicals. 3rd ed. New York, NY: Van Nostrand Reinhold Co., 1996. 1722]**PEER REVIEWED**

Fuel blending
[ITII. Toxic and Hazardous Industrial Chemicals Safety Manual. Tokyo, Japan: The International Technical Information Institute, 1988. 525]**PEER REVIEWED**

DENATURANT
[SRI]**PEER REVIEWED**

The largest chemical use for **toluene** is the production of benzene and urethane via hydrodealkylation.
[CHEMICAL PRODUCTS SYNOPSIS: Toluene, 1985]**PEER REVIEWED**

Used in production of drugs of abuse.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 3190]**PEER REVIEWED**

Manufacturers:

Amoco Corp., 200 East Randolph Drive, Chicago, IL 60601, (312)856-6111; Production site: Texas City, TX 77590
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

BP America, 200 Public Square, Cleveland OH 44114-2375. (216) 586-4141; Production sites: Alliance, LA 70037; Lima, OH 45804
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

CITGO Petrochemical Co., 6130 S. Yale Ave., Tulsa, OK 74136, (918)495-4000; Production sites: Corpus Christi, TX 78469; Lake Charles, LA 70601; Lemont, IL 60439-3659
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Coastal Refining and Marketing, 9 Greenway Plaza, Houston, TX 77046, (713)877-6559; Production site: Corpus Christi, TX 78403
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Coastal Eagle Point Co., 9 PO Box 1000, US Route 130& I295 Westville, NJ 08093, (609)853-3100;

Production site: Westville, NJ 08093
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Chevron Chemical Corp., 6001 Bollinger Canyon Rd., San Ramon, CA 94583, (925)842-5500; Production site: Port Arthur, TX 77460
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Dow Chemical USA, 2020 Dow Center, Midland, MI 48674, (517) 636-1000; Production site: Plaquemine, LA 70765
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Equistar Chemicals LP., One Houston Center, 1221 McKinney St., Suite 1600, Houston, TX 77010, (713)652-7300; Production sites: Alvin, TX 77511; Channelview, TX 77530; Corpus Christi, TX 78410
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Exxon Chemical Co., 13501 Katy Freeway, Houston, TX 77079, (281)871-6000; Production site: Baton Rouge, LA 70821
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Fina Oil and Chemical Co., PO Box 2159, Dallas, TX 75221-2159, (214) 750-2400; Production site: Port Arthur, TX 77460
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Hess Oil Virgin Islands Corp., Kings Hill Rd., P.O. Box 127 Kingshill, VI 00851-0127, (340)778-4000; Production site: St. Croix, VI 00850
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Koch Refining Co., PO Box 2256, Wichita, KS 67201, (316)828-5500; Production site: Corpus Christi, TX 78403
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Lyondell-CITGO Refining Co., 1200 Lawndale, Houston, TX 77017, (713)321-4111; Production site: Houston, TX 77252
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Marathon Ashland Petroleum LLC., 539 South Main St., Findlay, OH 45840-3295, (419) 422-2121; Production sites: Catlettsburg, KY 41129; Texas City, TX 77592-1191
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Mobil Chemical Co., 3225 Gallows Rd., Fairfax, VA 22037-0001, (703)846-3000; Production sites: Chalmette, LA 70043; Beaumont, TX 77704-3868
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Phillips Petroleum Co., Phillips Building, Bartlesville, OK 74004, (918)661-6600; Production site: Sweeney, TX 77480
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Phillips Puerto Rico Core Inc., Road 3 Route 710, Barrio Las Mareas Guayama PR 00785, (787)864-1515; Production site: Guayama, PR 00785
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Shell Chemical Co., One Shell Plaza, PO Box 2463, Houston, TX 77252-2463, (713)241-6161; Production site: Deer Park, TX 77536
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Sun Company Inc., 1801 Market St., Philadelphia, PA 19103, (800) 825-3535; Production sites: Marcus Hook, PA 19061; Toledo, OH 43693; Tulsa, OK 74102
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Texaco Refining and Marketing Inc., 10 Universal City Plaza, Universal City, CA 91608-1097, (818)505-2000; Production site: El Dorada, KS 67042
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Ultramar Diamond Corp., 6000 N. Loop 1604, W. San Antonio, TX 78249-1112, (210)592-2000; Production site: Three Rivers, TX 78071
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Valero Energy Corp., San Antonio Valero Tower, W 1H 10, San Antonio, TX 78229-4718, (210)370-2000; Production site: Houston, TX 77012-2408
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Methods of Manufacturing:

UNRECOVERED COMPONENT OF GASOLINE
[SRI]**PEER REVIEWED**

Catalytic reforming of petroleum steams accounts for 87% of total **toluene** production. An additional 9% is separated from pyrolysis gasoline produced in steam crackers during manufacture of ethylene and propylene ... coal-tar separation from coke ovens produces 1% of total **toluene** ... up to 2% of the **toluene** produced is obtained as a by-product from styrene manufacture.

[DCE/NCI; Monograph On Human Exposure To Chemicals In The Workplace: Toluene p.2-1 (1985)]**PEER REVIEWED**

(1) By catalytic reforming of petroleum. (2) By fractional distillation of coal tar light oil.
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 1997. 1113]**PEER REVIEWED**

General Manufacturing Information:

28th Highest-volume chemical produced in the USA (1995).
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 1997. 1113]**PEER REVIEWED**

Formulations/Preparations:

Research, reagent, nitration - all 99.8+%; Industrial: Contains 94+%, with 5% xylene and small amounts of benzene and nonaromatic hydrocarbons; 90/120: Less pure than industrial.
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Grades: Research 99.99%; Pure 99.98%
[Flick, E.W. Industrial Solvents Handbook. 3rd ed. Park Ridge, NJ: Noyes Publications, 1985. 48]**PEER REVIEWED**

Grades: 1st degree nitration; 2nd degree commercial; 90% solvent
[DCE/NCI; Monograph On Human Exposure To Chemicals In The Workplace: Toluene p.1-1 (1985)]**PEER REVIEWED**

Grade: (Usually defined in terms of boiling ranges) Pure, commercial, straw-colored, nitration, scintilation, industrial.
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 1997. 1113]**PEER REVIEWED**

Impurities:

... Commercial grades /of **toluene**/ usually contain small amounts of benzene as an impurity.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 3190]**PEER REVIEWED**

Technical grades (90-120 deg C boiling range) are less pure and may contain up to 25% benzene as well as other hydrocarbons.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47 80 (1989)]**PEER REVIEWED**

Commercial grades /of **toluene**/ can ... contain polynuclear aromatic hydrocarbons (PAH), including pyrene, fluoranthrene, and benzo[ghi]perylene.

[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Volumes I,II, III. Cincinnati, OH: ACGIH, 1991. 1568]**PEER REVIEWED**

Consumption Patterns:

CHEM INT FOR BENZENE, 55.3%; SOLVENT, 25.7%; CHEM INT FOR **TOLUENE** DIISOCYANATE, 7.3%; CHEM INT FOR BENZOIC ACID, 2.5%; CHEM INT FOR BENZYL CHLORIDE, 1.5%; OTHER, 7.7% (1981 NON-GASOLINE USE)
[SRI]**PEER REVIEWED**

Benzene, 46%; gasoline blending, 37%; solvent, 8%; **toluene** diisocyanate, 7%; miscellaneous chemicals, 2% (1985) /estimate/
[CHEMICAL PRODUCTS SYNOPSIS: Toluene, 1985]**PEER REVIEWED**

In the USA in 1981, the use of **toluene** as a solvent was second only to its use in benzene production via hydrodemethylation and accounted for about 26% of nonfuel consumption.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47 82 (1989)]**PEER REVIEWED**

Of the estimated 3.3 million tons of **toluene** produced in the USA in 1980, 44% was used to make benzene, 34% to make gasoline, 10% in solvents, 6% to make **toluene** diisocyanate, and 6% for miscellaneous use.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47 82 (1989)]**PEER REVIEWED**

U. S. Production:

(1981) 4.68X10+12 G (ALL USES, 93% CHEM GRADE)
[US INTERNATIONAL TRADE COMMISSION, WASH, DC 20436; SOC SERIES C/P-82-1]**PEER REVIEWED**

(1977) 1.50X10+12 G
[SRI]**PEER REVIEWED**

(1982) 1.54X10+12 G
[SRI]**PEER REVIEWED**

(1985) 2.30X10+12 g
[USITC. SYN ORG CHEM-U.S. PROD/SALES 1985 p.19]**PEER REVIEWED**

(1990) 6.21 billion lb
[Chem & Engineering News 70 (15): 17 (4/13/92)]**PEER REVIEWED**

(1991) 6.30 billion lb

[Chem & Engineering News 71 (15): 11 (4/12/93)]**PEER REVIEWED**

(1992) 5.81 billion lb
[Chem & Engineering News 72 (15): 13 (4/11/94)]**PEER REVIEWED**

(1993) 6.38 billion lb
[Chem & Engineering News 72 (15): 13 (4/11/94)]**PEER REVIEWED**

(1993) 2.276572X10+9 kg
[United States International Trade Commission. Synthetic Organic Chemicals - United States Production and Sales, 1993. USITC Publication 2810, Nov. 1994. Washington, D.C.,p. 3-13]**PEER REVIEWED**

U. S. Imports:

(1978) 1.92X10+11 G
[SRI]**PEER REVIEWED**

(1983) 2.73X10+11 G
[SRI]**PEER REVIEWED**

(1985) 1.57X10+8 gal
[BUREAU OF THE CENSUS. U.S. IMPORTS FOR CONSUMPTION AND GENERAL IMPORTS 1985 p.1-547]**PEER REVIEWED**

U. S. Exports:

(1978) 3.65X10+11 G
[SRI]**PEER REVIEWED**

(1983) 1.15X10+11 G
[SRI]**PEER REVIEWED**

(1985) 2.82X10+7 gal
[BUREAU OF THE CENSUS. U.S. EXPORTS, SCHEDULE E, 1985 p.2-70]**PEER REVIEWED**

Laboratory Methods:

Clinical Laboratory Methods:

NIOSH Method: 8002. Analyte: **Toluene**. Specimen: Venous blood, after 2 or more hours of exposure. Procedure: Gas chromatography, hydrogen-air flame ionization detector. The precision/RSD is 0.098 (1 ug/ml blood) and the recovery is 0.93 @ 2 ug/ml blood. The working range is 1 to 600 ug/ml. Applicability: **Toluene** is commonly found in trace amounts in humans working in the paint spray industry. Interferences: Ethanol in excess of the stated range increased blood **toluene** concentration. When substances other than the analytes are present in the blood, record their identities to determine possible interferences.
[U.S. Department of Health and Human Services, Public Health Service.

Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. 8002-1]**PEER REVIEWED**

A procedure for the determination of **toluene** in blood by the purge and trap method is described ... has a linear range which extends up to at least 1500 ug/l ... detection limit ... is estimated to be less than 7.5 ug/l ...
[Cocheo V et al; Am Ind Hyg Assoc 43 (12): 938-41 (1982)]**PEER REVIEWED**

An automated high performance liquid chromatographic method for the direct determination of urinary concentrations of p-methylhippuric acids, and metabolites of **toluene** is described. A mixed solution of 5 mM potassium phosphate monobasic/acetonitrile (90/10) was used as a mobile phase . The method is simple and specific. Urine can be analyzed without solvent extraction.
[Ogata M, Taguchi T; Int Arch Occup Environ Health 59 (3): 263-72 (1987)]**PEER REVIEWED**

Analytic Laboratory Methods:

Quantitative determination of 4 to 40 ppm **toluene** in water with precision of 10% using IR spectroscopy.
[Amer Water Works Assoc; Standard Methods for the Examination of Water and Waste Water 14th Ed (1976)]**PEER REVIEWED**

Quantitative method for detection of **toluene** in water by gas chromatography. Levels over 1 ppm can be detected.
[Amer Water Works Assoc; Standard Methods for the Examination of Water and Waste Water 14th Ed (1976)]**PEER REVIEWED**

TOLUENE WAS IDENTIFIED IN WASTE-CONTAMINATED SOIL AND CHEMICAL STILL BOTTOM EXTRACTS BY GC/FOURIER TRANSFORM INFRARED SPECTROMETRY.
[GURKA DF, BETOWSKI LD; ANAL CHEM 54: 1819 (1982)]**PEER REVIEWED**

TWENTY AQ INDUST EFFLUENTS CONTAINING POLLUTANTS WERE ANALYZED USING ISOTOPE DILN & GC/MASS SPECTROMETRY. **TOLUENE** WAS ONE OF THE POLLUTANTS.
[COLBY BN ET AL; INTERNATIONAL ENVIRONMENT & SAFETY FEB: 8 (1982)]**PEER REVIEWED**

NIOSH Method 1500. Analyte: **Toluene**. Matrix: Air. Procedure: Gas chromatography hydrogen-air flame ionization detector. For **toluene** this method has an estimated detection limit of 0.001 to 0.01 mg/sample with capillary column/sample. The overall precision/RSD is 0.011. Applicability: This method is intended for determining the OSHA-regulated hydrocarbons included within the boiling point range of n-pentane through n-octane. Interferences: At high humidity, breakthrough volumes may be reduced by as much as 50%.
[U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. 1500-1]**PEER REVIEWED**

NIOSH Method 4000. Analyte: **Toluene**. Procedure: Gas chromatography, hydrogen-air flame ionization detector. For **toluene** this method has an estimated detection limit of 0.01 mg/sample. The overall precision/RSD is 0.022. Applicability: The working range is 13 to 660 ppm (50 to 2500 mg/cu m) for a 4 hr sample. Interferences: None identified.
[U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. 4000-1]**PEER REVIEWED**

NIOSH Method 1501. Analyte: **Toluene**. Matrix: Air. Procedure: Gas chromatography, hydrogen-air flame ionization detector. For **toluene** this method has an estimated detection limit of 0.001 to 0.01 mg/sample with capillary column/sample. The overall precision/RSD is 0.011. Applicability: This method is for peak, ceiling and TWA determinations of aromatic hydrocarbons. Interferences: Use of the recommended column will prevent interferences by alkanes (less or equal to C10).
[U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. 1501-1]**PEER REVIEWED**

EPA Method 524.1. Purge-and-Trap Gas Chromatography/Mass Spectrometry. The method is applicable for the determination of volatile organic compounds in water, finished drinking water, raw source water, or drinking water in any treatment stage. For **toluene** the method has a detection limit of 0.08 ug/l and a standard deviation of 4.1%.
[USEPA; Methods for the Determination of Organic Compounds in Finished Drinking Water and Raw Source Water (1986)]**PEER REVIEWED**

EPA Method 524.2. Purge-and-Trap Gas Chromatography/Mass Spectrometry for the determination of volatile aromatic compounds in water including finished drinking water, raw source water, and drinking water in any treatment stage. For **toluene** the method has a detection limit of 0.11 ug/l and a relative standard deviation of 8.0% with a wide bore capillary column, and a method detection limit of 0.08 ug/l and a relative standard deviation of 5.9% with a narrow bore capillary column.
[USEPA; Methods for the Determinatioon of Organic Compounds in Finished Drinking Water and Raw Source Water (1986)]**PEER REVIEWED**

EPA Method 602. Purge-and-Trap Gas Chromatography with photoionization detection for the determination of purgeable aromatics including **toluene** in municipal and industrial discharges. Under the prescribed conditions for **toluene** the detection limit is 0.2 ug/l. The method is applicable for use in the concentration range from the method detection limit to 100 times that limit. Precision and method accuracy were found to be directly related to the concentration of the analyte essentially independent of the sample matrix.
[40 CFR 136 97/1/91)]**PEER REVIEWED**

EPA Method 624. Purge-and-Trap Gas Chromatography/Mass Spectrometry for the analysis of purgeable organics including **toluene** in the municipal and industrial discharges. Under the prescribed conditions, for **toluene** the method has a detection limit of 6.0 ug/l. Precision and method accuracy were

found to be directly related to the concentration of the analyte and essentially independent of the sample matrix.
[40 CFR 136 (7/1/91)]**PEER REVIEWED**

EPA Method 1624. Isotope Dilution Purge-and-Trap Gas Chromatography/Mass Spectrometry. This method is applicable for the determination of volatile organic compounds in municipal and industrial discharges. By adding a known amount of a labeled compound to every sample prior to purging, a correction of recovery of the pollutant can be made. If labeled compounds are not available, an internal standard method is used. Under the prescribed conditions, for both the labeled, and unlabeled ethylbenzene the method has a minimum detection level 10 ug/l.The established acceptance performance criteria at 20 ug/l is 6.2 ug/l for the standard deviation of the recovery, with the average recovery of 14.5 to 28.7 ug/l and the labeled cmpd recovery ranging from 4 to 193%.
[40 CFR 136 (7/1/91)]**PEER REVIEWED**

EPA Method 8020. Direct Injection or Purge-and-Trap Gas Chromatograpy with photoionization detection for the determination of aromatic volatile organics including **toluene** in solid waste. Under the prescribed conditions, for **toluene** the method has a detection limit of 0.2 ug/l. Precision and method accuracy were found to be directly related to the concentration of the analyte and essentially independent of the sample matrix.
[USEPA; Test Methods for Evaluating Solid Waste SW-846 (1986)]**PEER REVIEWED**

EPA Method 8240. Gas Chromatography/Mass Spectrometry for the determination of volatile Organics. This method can be used to quantify most volatile organic compounds including **toluene** that have boiling points below 200 deg C and are insoluble or slightly soluble in water. The detection limit is not given. Precision and method accuracy were found to be directly related to the concentration of the analyte and essentially independent of the sample matrix.
[USEPA; Test Methods for Evaluating Solid Waste SW-846 (1986)]**PEER REVIEWED**

EPA Method 502.2: Purge-and-Trap Capillary Column Gas Chromatography with Photoionization and Electrolytic Conductivity Detectors in Series. The method is applicable for the determination of volatile organic compounds in finished drinking water, raw source water, or drinking water in any treatment stage. For **toluene** the method has a detection limit of 0.01 ug/l, a percent recovery of 99%, and a standard deviation of 1.9 using the photoionization detector.
[USEPA; Methods for the Determination of Organic Compounds in Finished Drinking Water and Raw Source Water (1986)]**PEER REVIEWED**

EPA Method 502.1. Purge and Trap Gas Chromatography with a halogen-specific detector for the determination of halogenated volatile compounds including **toluene** in finished drinking water, raw source water, or drinking water in any treatment stage. Under the prescribed conditions for **toluene**, the method detection limit is 0.02 ug/l.
[USEPA; Methods for the Determination of Organic Compounds in Finished Drinking Water and Raw Source Water (1986)]**PEER REVIEWED**

AOB Method OA-002-1. Volatile Organic Compounds by GC/MS Analysis of Tenax/CMS Cartridge and Summa Canister Samples. No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version

1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VA-001-1. Volatile Organic Compounds (VOCs) in Air Sampled by Sorbent Tubes and Analyzed by Purge and Trap GC. No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VA-003-1. Volatile Organic Compounds (VOCs) in Air by Portable GC/PID. No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VA-005-1. Volatile Organic Compounds (VOCs) in Ambient Air by Purge and Trap Gas Chromatography. No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VA-006-1. Volatile Organic Compounds (VOCs) in Ambient Air by Direct Portable GC/PID. No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VA-007-1. Volatile Organic Compounds (VOCs) in Ambient Air by GC/PID, GC/PID/FID, or GC/FID. No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VA-008-1. Volatile Organic Compounds (VOCs) in Ambient Air by Portable GC/PID with Direct Sampling via Pump and Sample Loop. No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VG-001-1. Volatile Organics in Soil Gas - Adsorbent Tube Method. No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VG-006-1. Volatile Organic Compounds (VOCs) in Ambient Air by Purge and Trap GC. No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VG-007-1. Halogenated and Aromatic Volatile Organic Compounds (VOCs) in Air and Soil Gas Sampled by Sorbent Tubes and Analyzed by Purge and Trap GC/ELCD/PID. No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VG-008-1 . Volatile Organic Compounds (VOCs) in Soil Gas sampled by Tenax Tubes and Analyzed by Thermal Desorption GC/PID/ELCD. No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VG-010-1. Volatile Organic Compounds (VOCs) in Soil Gas by Direct Portable GC. No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AREAL Method IP-1A . Determination of Volatile Organic Compounds (VOCs) in Indoor Air Using Stainless Steel Canisters. No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AREAL Method IP-1B . Determination of Volatile Organic Compounds (VOCs) in Indoor Air using Solid Absorbent Tubes. No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AREAL Method TO-1 . Determination of Volatile Organic Compounds in Ambient Air using Tenax Adsorption and Gas Chromatography/Mass Spectrometry (GC/MS). No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AREAL Method TO-2 . Determination of Volatile Organic Compounds In Ambient Air by Carbon Molecular Sieve Adsorption and Gas Chromatography/Mass Spectrometry (GC/MS). No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AREAL Method TO-14. Determination of Volatile Organic Compounds (VOCs) in Ambient Air using SUMMA Passivated Canister Sampling and Gas Chromatographic Analysis. No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

Sampling Procedures:

... Personal dosimeter type badge monitor collects organic vapors ... /for analysis/ using gas chromatographic techniques ... sampled over the range of 0.5 ppm-1100 ppm /organic vapors/
[Lautenberger WJ et al; Am Ind Hyg Assoc J 41 (10): 737-47 (1980)]**PEER REVIEWED**

NIOSH Method 1500. Analyte: **Toluene**. Matrix: Air. Sampler: Solid sorbent tube (coconut shell charcoal, 100 mg/50 mg). Flow Rate: 0.20 l/min. Sample Size: 8 liters. Shipment: No special precautions. Sample Stability: At least 2 weeks.
[U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. 1500-1]**PEER REVIEWED**

NIOSH Method 4000. Analyte: **Toluene**. Sampler: Passive (activated carbon). Shipment: Transfer sorbent to septum-capped vial; otherwise routine. Sample Stability: At least 2 weeks @ 25 deg C if stored in septum-capped vial.
[U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. 4000-1]**PEER REVIEWED**

NIOSH Method 8002. Analyte: **Toluene**. Specimen: Venous blood, after 2 or more hrs of exposure. Shipment: Air express @ 4 deg C. Sample Stability: Stable @ 4 deg C for 3 weeks.
[U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. 8002-1]**PEER REVIEWED**

NIOSH Method 1501. Analyte: **Toluene**. Matrix: Air. Sampler: Solid sorbent tube (coconut shell charcoal, 100 mg/50 mg). Flow Rate: Less or equal to 0.20. Sample Size: 8-liters. Shipment: No special precautions. Sample Stability: Not determined.
[U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. 1501-1]**PEER REVIEWED**

Special References:

Special Reports:

REVIEW: BENIGNUS VA; NEUROTOXICOLOGY (PARK FOREST SOUTH, ILL) 2 (3): 567 (1981). REVIEW ON HEALTH EFFECTS OF **TOLUENE**, PARTICULARLY WITH RESPECT TO ITS

NEUROTOXIC EFFECTS IN HUMANS AND LAB ANIMALS.

NIOSH; Criteria Document: **Toluene** (1973) DHEW Pub. NIOSH 73-11023

USEPA; Ambient Water Quality Doc: **Toluene** (1980) EPA 440/5-80-075

NAS/NRC; The Alkyl Benzenes 384 pp (1981)

USEPA; Health Assessment Document: **Toluene** (1982) EPA-800/8-82-008

TSCA CHIPs present a preliminary assessment of **toluene**'s potential for injury to human health & the environment (available at EPA's TSCA Assistance Office: (202) 554-1404.

Environment Canada; Tech Info for Problem Spills: **Toluene** (Draft) (1981)

Carlton WW et al; J Am Coll Toxicol 6 (1): 77-120 (1987). Final Report on the Safety Assessment of **Toluene**.

DHHS/ATSDR; Toxicological Profile for **Toluene** (Update) (1994) ATSDR/TP-93/14

DHHS/NTP; Toxicology & Carcinogenesis Studies of **Toluene** in F344/N Rats and B6C3F1 Mice Technical Report Series No. 371 (1990) NIH Publication No. 90-2826

Synonyms and Identifiers:

Synonyms:

ANTISAL 1A
PEER REVIEWED

BENZENE, METHYL-
PEER REVIEWED

Caswell no 859
PEER REVIEWED

CP 25
PEER REVIEWED

METHACIDE
PEER REVIEWED

METHANE, PHENYL-
PEER REVIEWED

METHYLBENZENE
PEER REVIEWED

METHYLBENZOL
PEER REVIEWED

NCI-C07272
PEER REVIEWED

PHENYLMETHANE
PEER REVIEWED

TOLUEEN (DUTCH)
PEER REVIEWED

TOLUEN (CZECH)
PEER REVIEWED

TOLUOL
PEER REVIEWED

TOLUOLO (ITALIAN)
PEER REVIEWED

Formulations/Preparations:

Research, reagent, nitration - all 99.8+%; Industrial: Contains 94+%, with 5% xylene and small amounts of benzene and nonaromatic hydrocarbons; 90/120: Less pure than industrial.
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Grades: Research 99.99%; Pure 99.98%
[Flick, E.W. Industrial Solvents Handbook. 3rd ed. Park Ridge, NJ: Noyes Publications, 1985. 48]**PEER REVIEWED**

Grades: 1st degree nitration; 2nd degree commercial; 90% solvent
[DCE/NCI; Monograph On Human Exposure To Chemicals In The Workplace: Toluene p.1-1 (1985)]**PEER REVIEWED**

Grade: (Usually defined in terms of boiling ranges) Pure, commercial, straw-colored, nitration, scintilation, industrial.
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 1997. 1113]**PEER REVIEWED**

Shipping Name/ Number DOT/UN/NA/IMO:

UN 1294; **Toluene**

IMO 3.2; **Toluene**

Standard Transportation Number:

49 093 05; **Toluene**

49 093 56; **Toluene** (**toluol**), reclaimed solvents, derived from the use of printing inks, consisting of 70% recycled **toluol** and not more than 30% lactol spirits, textile spirits and mineral spirits

49 060 10; **Toluene** (**toluol**), mixed with aluminum alkyls, not to exceed 20% (aluminum alkyl)

EPA Hazardous Waste Number:

U220; A toxic waste when a discarded commercial chemical product or manufacturing chemical intermediate or an off-specification commercial chemical product or manufacturing chemical intermediate.

F005; A hazardous waste from nonspecific sources when a spent solvent.

RTECS Number:

NIOSH/XS5250000

Administrative Information:

Hazardous Substances Databank Number: 131

Last Revision Date: 20010131

Last Review Date: Reviewed by SRP on 1/29/2000

Update History:

Complete Update on 01/31/2001, 2 fields added/edited/deleted.
Complete Update on 09/12/2000, 1 field added/edited/deleted.
Complete Update on 08/04/2000, 91 fields added/edited/deleted.
Field Update on 06/12/2000, 1 field added/edited/deleted.
Field Update on 06/12/2000, 1 field added/edited/deleted.
Field Update on 02/02/2000, 1 field added/edited/deleted.
Field Update on 09/21/1999, 1 field added/edited/deleted.
Complete Update on 05/04/1999, 1 field added/edited/deleted.
Complete Update on 03/29/1999, 3 fields added/edited/deleted.
Field Update on 03/25/1999, 1 field added/edited/deleted.
Field Update on 03/19/1999, 1 field added/edited/deleted.
Complete Update on 02/24/1999, 1 field added/edited/deleted.
Complete Update on 01/20/1999, 3 fields added/edited/deleted.
Field Update on 12/18/1998, 1 field added/edited/deleted.
Complete Update on 11/12/1998, 1 field added/edited/deleted.
Complete Update on 09/11/1998, 1 field added/edited/deleted.
Complete Update on 06/02/1998, 1 field added/edited/deleted.
Complete Update on 03/25/1998, 4 fields added/edited/deleted.
Field Update on 02/25/1998, 1 field added/edited/deleted.
Field Update on 10/17/1997, 1 field added/edited/deleted.
Field Update on 09/08/1997, 5 fields added/edited/deleted.
Complete Update on 03/27/1997, 2 fields added/edited/deleted.
Complete Update on 02/26/1997, 1 field added/edited/deleted.
Complete Update on 06/11/1996, 1 field added/edited/deleted.
Complete Update on 05/10/1996, 1 field added/edited/deleted.
Complete Update on 04/18/1996, 2 fields added/edited/deleted.
Complete Update on 04/16/1996, 7 fields added/edited/deleted.
Complete Update on 01/18/1996, 1 field added/edited/deleted.

Complete Update on 06/09/1995, 1 field added/edited/deleted.
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Complete Update on 01/24/1995, 1 field added/edited/deleted.
Complete Update on 12/19/1994, 1 field added/edited/deleted.
Complete Update on 11/18/1994, 2 fields added/edited/deleted.
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Complete Update on 06/08/1994, 1 field added/edited/deleted.
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Complete Update on 03/25/1994, 1 field added/edited/deleted.
Complete Update on 09/15/1993, 1 field added/edited/deleted.
Complete Update on 08/17/1993, 1 field added/edited/deleted.
Complete Update on 08/07/1993, 1 field added/edited/deleted.
Complete Update on 08/04/1993, 1 field added/edited/deleted.
Complete Update on 04/30/1993, 1 field added/edited/deleted.
Complete Update on 02/05/1993, 1 field added/edited/deleted.
Field update on 12/11/1992, 1 field added/edited/deleted.
Complete Update on 11/20/1992, 1 field added/edited/deleted.
Complete Update on 09/18/1992, 1 field added/edited/deleted.
Complete Update on 09/14/1992, 73 fields added/edited/deleted.
Complete Update on 08/17/1992, 73 fields added/edited/deleted.
Field Update on 05/29/1992, 1 field added/edited/deleted.
Field Update on 04/16/1992, 1 field added/edited/deleted.
Field Update on 01/13/1992, 1 field added/edited/deleted.
Field Update on 09/10/1991, 1 field added/edited/deleted.
Complete Update on 07/08/1991, 1 field added/edited/deleted.
Complete Update on 05/31/1991, 1 field added/edited/deleted.
Complete Update on 10/22/1990, 9 fields added/edited/deleted.
Field Update on 05/14/1990, 1 field added/edited/deleted.
Field Update on 01/15/1990, 1 field added/edited/deleted.
Complete Update on 01/11/1990, 7 fields added/edited/deleted.
Field Update on 05/05/1989, 1 field added/edited/deleted.
Complete Update on 09/21/1988, 95 fields added/edited/deleted.
Complete Update on 05/31/1985

Record Length: 261364

TOLUENE

CASRN: 108-88-3

For other data, click on the Table of Contents

Human Health Effects:

Evidence for Carcinogenicity:

Evaluation: There is inadequate evidence for the carcinogenicity of **toluene** in humans. There is evidence suggesting lack of carcinogenicity of **toluene** in experimental animals. Overall evaluation: **Toluene** is not classifiable as to its carcinogenicity to humans (Group 3).
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V71 855 (1999)]**PEER REVIEWED**

CLASSIFICATION: D; not classifiable as to human carcinogenicity. BASIS FOR CLASSIFICATION: No human data and inadequate animal data. **Toluene** did not produce positive results in the majority of genotoxic assays. HUMAN CARCINOGENICITY DATA: None.
[U.S. Environmental Protection Agency's Integrated Risk Information System (IRIS) on Toluene (108-88-3) Available from: http://www.epa.gov/ngispgm3/iris on the Substance File List as of March 15, 2000]**PEER REVIEWED**

A4. A4= Not classifiable as a human carcinogen.
[American Conference of Governmental Industrial Hygienists. TLVs and BEIs. Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. Cincinnati, OH. 2000. 67]**QC REVIEWED**

Human Toxicity Excerpts:

Among 61 painters inhaling 100-1100 ppm **toluene** for 2 wk to 5 yr, depressed erythrocyte counts with elevated hemoglobin, mean corpuscular volumes, and elevated mean corpuscular hemoglobin were found in 5% to 30% compared with groups of 73-395 workers not known to be exposed to **toluene**; differential leukocyte counts were not significantly different between the **toluene**-exposed and the reference workers.
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Volumes I,II, III. Cincinnati, OH: ACGIH, 1991. 1573]**PEER REVIEWED**

... **TOLUENE** CAUSES DEFATTING OF SKIN WITH SUBSEQUENT DANGER OF DRYNESS, FISSURING AND SECONDARY INFECTION.
[International Labour Office. Encyclopedia of Occupational Health and Safety. Volumes I and II. New York: McGraw-Hill Book Co., 1971. 1414]**PEER REVIEWED**

... SUDDEN DEATH AMONG "SNIFFERS" MAY BE ATTRIBUTED TO LETHAL CARDIAC ARRHYTHMIAS FOLLOWING SENSITIZATION OF THE MYOCARDIUM.
[Hamilton, A., and H. L. Hardy. Industrial Toxicology. 3rd ed. Acton, Mass.: Publishing Sciences Group, Inc., 1974. 276]**PEER REVIEWED**

... PERMANENT ENCEPHALOPATHY ... /IN/ MAN WHO INHALED **TOLUENE** REGULARLY FOR OVER 14 YR /WAS DESCRIBED/.
[American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices. 5th ed. Cincinnati, OH:American Conference of Governmental Industrial Hygienists, 1986. 578]**PEER REVIEWED**

VAPORS OF **TOLUENE** CAUSE NOTICEABLE SENSATION OF IRRITATION TO HUMAN EYES AT 300-400 PPM IN AIR, BUT EVEN AT 800 PPM IRRITATION IS SLIGHT. ... IN HUMAN VOLUNTEERS EXPOSED TO CONCN AS HIGH AS 800 PPM ... DILATION OF PUPILS & IMPAIRMENT OF REACTION IN ASSOCIATION WITH FATIGUE AT END OF 8 HR, ALSO SLIGHT PALLOR OF FUNDI.
[Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986. 927]**PEER REVIEWED**

Metabolic acidosis with a high "anion gap" in 2 patients who had been sniffing **toluene**.
[Reynolds, J.E.F., Prasad, A.B. (eds.) Martindale-The Extra Pharmacopoeia. 28th ed. London: The Pharmaceutical Press, 1982. 1455]**PEER REVIEWED**

A report of 2 children who sniffed glue containing **toluene**. One of the children became comatose after an episode of "sniffing" which lasted for several hours. Adverse effects included reduced appetite, nightmares, vertical nystagmus, and incoordination.
[Reynolds, J.E.F., Prasad, A.B. (eds.) Martindale-The Extra Pharmacopoeia. 28th ed. London: The Pharmaceutical Press, 1982. 1455]**PEER REVIEWED**

WORKERS IN PHARMACEUTICAL PLANT IN FRANCE EXPOSED TO **TOLUENE** DEVELOPED LEUKOPENIA, & NEUTROPENIA. WITHIN 6 MO, THOSE AFFECTED SHOWED INCR IN CLOTTING TIME & DECR IN PROTHROMBIN LEVEL ...
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1329]**PEER REVIEWED**

PERIPHERAL BLOOD LYMPHOCYTES FROM 32 MALE ROTOGRAVURE WORKERS SHOWED NO SIGNIFICANT DIFFERENCE FROM CONTROLS IN FREQUENCY OF CHROMOSOME ABERRATIONS & SISTER CHROMATID EXCHANGES.
[MAKI-PAAKKANEN J ET AL; J TOXICOL ENVIRON HEALTH 6: 775 (1980)]**PEER REVIEWED**

Patients (3) with history of recurrent **toluene** abuse were hospitalized and severe metabolic acidosis, electrolyte abnormalities, hypoalkemia, and muscular weakness were present. Distal renal tubular acidosis was believed to be present in 2/3 patients.

[Fiscman CM, Oster JR; Am Med Assoc 241 (16): 1713-15 (1979) as cited in NRC; Alkyl Benzenes p.284 (1981)]**PEER REVIEWED**

Child of a mother with a 14 year history of solvent abuse showed symptoms of fetal alcohol syndrome.
[Toutant C, Lippman S; Lancet 1 (8130): 1356 (1979)]**PEER REVIEWED**

A 27-year-old male developed cerebral and cerebellar atrophy over a period of five years of extensive glue sniffing. He also developed bilateral optic atrophy with blindness and severe sensorineural hearing loss.
[Ehyai A, Freemon FR; J Neural Neurosurg Psychiatry 46 (4): 349-51 (1983)]**PEER REVIEWED**

Toluene appears to produce reversible effects upon liver, renal, and nervous systems. ... The nervous system appears to be the most sensitive to the effects of **toluene**. ... High level **toluene** exposures produced incoordination, ataxia, unconsciousness and eventually, death. Lower level acute exposures in man produce dizziness, exhilaration and confusion. Activity level has been inadequately studied. Schedule controlled behaviors have been reported to produce inverted U-shaped concentration-effect curves on response rate measures. Alterations at levels as low as 150 ppm have been reported when appetitive contingencies are used. Very few studies of the nervous system have been performed at levels below 1000 ppm and most of the results were inconclusive. ...
[Benignus VA; Neurobehav Toxicol Teratol 3 (4): 407-15 (1981)]**PEER REVIEWED**

Lethal levels 1.0 mg%; 10.0 ug/ml
[Winek, C.L. Drug and Chemical Blood-Level Data 1985. Pittsburgh, PA: Allied Fischer Scientific, 1985.]**PEER REVIEWED**

IN EXPERIMENTS IN VITRO, **TOLUENE** DID NOT CHANGE NUMBER OF SISTER-CHROMATID EXCHANGES OR THE NUMBER OF CHROMOSOMAL ABERRATIONS IN HUMAN LYMPHOCYTES.
[GERNER-SCMIDT P, FRIEDRICH U; MUTATION RESEARCH 58: 313 (1978)]**PEER REVIEWED**

A 28 yr old painter who was believed to be a habitual **toluene** sniffer was admitted to Chiba Emergency Medical Center on several occasions. Symptoms included: Tremors of the upper extremeties, staggering of gait, slurred speech, slight mental deterioration, pendular nystagmus, bradycardia, mild tremor of the leg, action myoclonus, and head and trunchal titubation. There was no dysmetria. The involuntary movements were classified as hyperkinesie volitionnelle. Muscle tone was hypotonic. Muscle weakness and atrophy were not seen. Deep tendon reflexes were all exaggerated, but there was no pathological reflex. He showed wide-based ataxic gait. Sensory and autonomic functions were normal. Blood, urine and cerebrospinal fluid analysis appeared normal. Electroencephalography showed 40-50 uV, 9-10 c/s alpha waves with a few fast waves. Brain CT scan revealed a moderate enlargement of the lateral and third ventricles. Surface electromyography was performed on the proximal musculature of the arm. 3 c/s reciprocal rhythmical grouping discharges were found at the terminal phase of the elbow bending. The tremor was diminished by 20 minutes ischemic compression test of the arm. With respect to therapy, clonazepam was useful for hyperkinesie volitionnelle. He became able to drink a cup of water without spilling it by his own hands, and was discharged from hospital on April 3rd, 1981. It was believed that he was a habitual sniffer to **toluene**. On June 30th, 1983 he was found comatose. On admission to Chiba

Emergency Medical Center, his breath smelt of **toluene**. His blood **toluene** level was 7.53 ppm, and urinary hippuric acid concentration was 9,500 mg/l. He died on July 9th, 1983, because of disseminated intravascular coagulation, multiple organ failure and perforation of the terminal ileum. Autopsy was performed and neuropathological findings were as follows. 1) Diffuse demyelination and gliosis of the cerebral and cerebella white matter. 2) Marked loss of Purkinje cells of the cerebellum. 3) Astrocytic proliferation of the dentate fugal system and inferior olivary nucleus of medulla. ...
[Arai K et al; Brain Nerve Tokyo 38 (12): 1181-86 (1986)]**PEER REVIEWED**

Autopsy findings on a man who fell from a height due to acute **toluene** poisoning while painting are described. Gas chromatographic examination revealed that the **toluene** concentrations of his blood, lung, liver and brain were 48, 35, 65 and 80 ug/g, respectively. These **toluene** levels were not enough to be definitely lethal, but were enough to anesthetize the central nervous system.
[Takeichi S et al; Forensic Sci Int 32 (2): 109-16 (1986)]**PEER REVIEWED**

The psychological performance of 43 rotogravure printers exposed to a mean time- weighted average of 117 ppm **toluene** for a mean time period of 21.7 yr was compared to that of 31 offset printers with a mean working period of 23 yr. The offset printers were exposed to mixtures of aliphatic hydrocarbons or ethyl acetate (amounts not given) for a total of 10 to 60 min daily. Drinking habits were considered in grouping the workers. The test battery consisted of standardized tests for verbal and visual cognition and memory, perceptual motor speed, and psychomotor abilities. Performances of the two printer groups were similar with rotogravure printers having statistically significant lower scores on tests measuring visual cognitive abilities. Mean test performances indicated that drinking habits did not explain the impairment of visual cognitive abilities.
[Hanninen H et al; Int Arch Occupat Environ Health 59 (5): 475-83 (1987)]**PEER REVIEWED**

Acute poisoning may result from exposure to high concn of **toluene**; A /CNS depressant/ effect is produced. Human death has resulted from exposure to 10,000 ppm. **Toluene** is more acutely toxic than benzene; however, severe blood disorders of the type associated with benzene are not reported. Inhalation of 200 ppm has affected the CNS in humans.
[Cleland, J.G., G.L. Kingsbury. Multimedia Environmental Goals for Environmental Assessment. Volume 1. EPA-600/7-77-136a. Research Triangle Park, NC: EPA, Nov. 1977.,p. E-146]**PEER REVIEWED**

Vapors irritate eyes and upper respiratory tract; Cause dizziness, headache, anesthesia, and respiratory arrest. Liquid irritates eyes. If aspirated, causes coughing, gagging, distress, and rapidly developing pulmonary edema. If ingested causes vomiting, griping, diarrhea, and depressed respiration. Kidney and liver damage may follow ingestion.
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

In recent years some youngsters have been indulging in what is called thinner inhalation, posing a serious social problem. Organic solvents have also been widely used industrially as adhesives or degreasing and rinsing agents, generating a kind of occupational disease which has become a medical problem. Some

school children who refuse to go to school complaining of headache, head heaviness, blurred vision, diplopia, or dizziness, may actually have **toluene** toxicosis caused by the adhesive they use in constructing plastic models. /An examination of/ 35 such patients neurogically, found some impairment in the cerebellar cortex, cerebellar nuclei, or efferent pathways. This report is presented to invite comments from other researchers.
[Sakata E et al; Pract Otal Kyoto 79 (12): 1999-2013 (1986)]**PEER REVIEWED**

Severe, acute **toluene** intoxication in two workers was described. Special attention was paid to the metabolism of **toluene** in man and to the choice of reference parameters to monitor intoxication. The men had tiled a small swimming pool to be used for exercise programs in a rehabilitation clinic. They had used a special glue to make the joints of cement between the tiles resistant to bleaching solution; the next day they removed the excess glue using **toluene**. One worker was exposed for 2 hours and the other for 3 hours. Both were overcome with the fumes, and were found lying at the bottom of the pool. Symptoms included stupefaction, paresis, and amnesia. Patient-A had mucosal irritation of the eyes and slurred speech. He was stuporose and unable to walk or sit. His amnesia lasted for about 3 hours. Patient-B had mucosal irritation of the eyes, was drowsy, and was just able to walk. He had normal speech and complained of headache. The duration of his amnesia was about 2.5 hours. Solid evidence for **toluene** exposure was provided by the blood **toluene** concentration. The concentration 2 hours after exposure was 4.1 mg/l in patient-A and 2.2 mg/l in patient-B.
[Meulenbelt J et al; Br J Ind Med 47 (6): 417-20 (1990)]**PEER REVIEWED**

The memory sequelae for a group of female workers accidentally exposed to organic solvents were examined retrospectively to evaluate complaints of residual memory impairment. The subjects included seven employees (mean age 32.1 years) who agreed to retesting and who had been severely intoxicated by exposure to **toluene** and aliphatic hydrocarbons found in adhesives used in the manufacture of tennis balls. They were compared to eight workers (mean age 33.7 years) who were solvent exposed but not affected by the accident and ten workers (mean age 36.6 years) who had no exposure. Acute symptoms included faintness, nausea, vomiting, and headache. Complaints of impaired memory, personality changes, and loss of confidence persisted 8 months after exposure. Memory testing was first performed 2 months after exposure, with the follow up 6 months later to assess recovery. The three memory tasks included paired associate task, serial position task, and Brown-Peterson task. The subjects showed normal patterns of performance on tests of learning and short term and long term memory, but demonstrated marked difficulties when attention had to be divided between two resource competing tasks. The clearest evidence of impairment was observed in the Brown-Peterson task, where the acute group showed a significantly greater increase in word recall omission after periods of counting backwards in threes. The magnitude of the memory sequelae was not correlated with scores of self rated depression. It was concluded that solvent intoxication can cause neuropsychological sequelae lasting more than 8 months; memory tasks could prove useful in identifying memory impairment in other occupationally exposed groups.
[Stollery BT, Flindt MLH; Scand J Work, Environ, Health 14 (1): 45-8 (1988)]**PEER REVIEWED**

In a cross-sectional study of 181 male workers of a rotogravure printing plant, most of whom were exposed to **toluene** levels well above the GDR threshold limit values, 55 subjects revealed pathological liver screening values (activities of serum aspartate aminotransferase, alanine aminotransferase, gamma

glutamyltransferase; liver size). The differential diagnostic examination showed in 51 of these 55 subjects an association with competing factors such as alcohol abuse (78%) and overweight (40%), to a slight extent disorders of fat and carbohydrate metabolism and of the gallbladder. Drug intake did not play any role. The variance and regression analyses of the biochemical data have shown that alcohol significantly and considerably increases the activities of all three enzymes tested. Bodyweight had a similar, but less pronounced, significant effect. On the other hand, in subjects with a higher alcohol intake the activities of liver enzymes in highly **toluene** exposed subgroups were significantly and clearly lower than among slightly **toluene** exposed workers.
[Boewer C et al; Int Arch Occup Environ Health 60 (3): 181-6 (1988)]**PEER REVIEWED**

General health effects include lethality, growth, morbidity, liver and kidney damage and miscellaneous effects. Neurobehavioral effects include epidemiological and clinical findings, activity and sleep, performance and learning, electrophysiological effects. Evaluation and synthesis of data is included. It was concluded that low level exposure to **toluene** has its primary effect on the CNS. From a systematic or general point of view it is not clear what this effect is. Both depressant and excitatory effects (possibly concentration dependent) were reported as well as other kinds of results. Other health effects were not life threatening at any exposure level short of that producing lethality. Effects were reversible even at extremely high exposure levels for very long durations.
[Benignus VA; Neurotoxicol 2 (3): 567-88 (1981)]**PEER REVIEWED**

Toluene embryopathy is characterized by microcephaly, central nervous system dysfunction, attentional deficits and hyperactivity, developmental delay with greater language deficits, minor craniofacial and limb anomalies, and variable growth deficiency. Previously, three affected children, born to women who inhaled **toluene** regularly throughout pregnancy, have been reported. Two more cases are described emphasizing the importance of **toluene** as a potential human teratogen.
[Hersh JH; J Med Genet 26 (5): 333-7 (1989)]**PEER REVIEWED**

Neurobehavioral tests were undertaken by 30 female workers exposed to **toluene** and matched controls with low occupational exposure to **toluene**. The environmental air levels (TWA) of **toluene** was 88 ppm for the exposed workers and 13 ppm for the controls. The **toluene** in blood concentrations for the exposed workers was 1.25 mg/l and for the controls 0.16 mg/l. Statistically significant differences between workers exposed to **toluene** and controls in neurobehavioral tests measuring manual dexterity (grooved peg board), a visual scanning (trail making, visual reproduction, Benton visual retention, and digit symbol), and verbal memory (digit span) were observed. Further, the performance at each of these tests was related to time weighted average exposure concentrations of air **toluene**. The workers exposed to **toluene** had no clinical symptoms or signs. The question arises as to whether these impairments in neurobehavioral tests are reversible or whether they could be a forerunner of more severe damage.
[Foo SC et al; BR J Ind Med 47 (7): 480-4 (1990)]**PEER REVIEWED**

When compared with benzene, **toluene** has little to no effect on immunocompetence. However, it should be noted that **toluene** exposure effectively attenuates the immunotoxic effects of benzene (probably because of competition for metabolic enzymes).
[Klaassen, C.D., M.O. Amdur, Doull J. (eds.). Casarett and Doull's Toxicology. The Basic Science of Poisons. 5th ed. New York, NY: McGraw-Hill, 1995. 380]**PEER REVIEWED**

Neutral organic solvents such as ... **toluene** ... cause pain on contacting the eye, and examination after a generous splash of solvent shows dulling of the cornea. The epithelium will show punctate staining with fluorescein. The damage appears to be scattered loss of epithelial cells due to solution of some of the fats that occur in these cells.
[Klaassen, C.D., M.O. Amdur, Doull J. (eds.). Casarett and Doull's Toxicology. The Basic Science of Poisons. 5th ed. New York, NY: McGraw-Hill, 1995. 586]**PEER REVIEWED**

Toxicities associated with **toluene**: CNS depression, syncope, coma, cardiac arrhythmias and sudden death, ataxia, convulsions, rhabdomyolysis, increased creatine phosphokinase, abdominal pain, nausea, vomiting, hematemesis, peripheral neuropathy, paresthesias, encephalopathy, optic neuropathy, cerebella ataxia, distal renal tubular acidosis, hyperchloremia, hypokalemia, azotemia, hypophosphatemia, hematuria, proteinuria, pyruria, normalities, decreased cognitive function, fatal overdose. /From table/
[Ellenhorn, M.J., S. Schonwald, G. Ordog, J. Wasserberger. Ellenhorn's Medical Toxicology: Diagnosis and Treatment of Human Poisoning. 2nd ed. Baltimore, MD: Williams and Wilkins, 1997. 1494]**PEER REVIEWED**

Women workers exposed to high air concentrations of **toluene** (50-150 ppm) appeared to have a higher incidence of spontaneous abortion than a similar group of women with no occupational exposure to **toluene**.
[Ellenhorn, M.J., S. Schonwald, G. Ordog, J. Wasserberger. Ellenhorn's Medical Toxicology: Diagnosis and Treatment of Human Poisoning. 2nd ed. Baltimore, MD: Williams and Wilkins, 1997. 166]**PEER REVIEWED**

Maternal spray paint or glue sniffing leads to maternal complications including renal tubular acidosis, hypokalemia, hypocalcemia, cardiac arrhythmias, rhabdomyolysis, and premature labor. Premature **toluene** exposure leads to a characteristic pattern of anomalies similar to findings in infants exposed to alcohol in utero, consisting of an increased incidence of malformations, poor growth, and developmental delays.
[Ellenhorn, M.J., S. Schonwald, G. Ordog, J. Wasserberger. Ellenhorn's Medical Toxicology: Diagnosis and Treatment of Human Poisoning. 2nd ed. Baltimore, MD: Williams and Wilkins, 1997. 166]**PEER REVIEWED**

Eye and upper airway irritation occurred after a 6.5 hr exposure to an air level of 100 ppm (377 mg/cu m) **toluene**, and lachrymation was seen at 500 mg/cu m.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47 101 (1989)]**PEER REVIEWED**

Volunteers exposed to 100 ppm (377 mg/cu m) **toluene** for 6 hr/day for four days suffered from subjective complaints of headache, dizziness and a sensation of intoxication. In subjects exposed to 750 mg/cu m for 8 hr, fatigue, muscular weakness, confusion, impaired coordination, enlarged pupils and accommodation disturbances were experienced; at about 3000 mg/cu m, severe fatigue, pronounced nausea, mental confusion, considerable incoordination with staggering gait and strongly affected pupillary light reflexes were observed. After exposure at the high level, muscular fatigue, nervousness and insomnia lasted for several days. Heavy accidental exposure leads to coma.

[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47 101 (1989)]**PEER REVIEWED**

Humans exposed to concentrations of **toluene** of between 200-800 ppm may experience respiratory and ocular irritation.
[Sullivan, J.B. Jr., G.R. Krieger (eds.). Hazardous Materials Toxicology-Clinical Principles of Environmental Health. Baltimore, MD: Williams and Wilkins, 1992. 1090]**PEER REVIEWED**

Children with microcephaly, minor craniofacial and limb anomalies, central nervous system defects, attention disorders, developmental delay, learning disorders, and language deficits were born to mothers who abuse **toluene** by inhalation during pregnancy.
[Sullivan, J.B. Jr., G.R. Krieger (eds.). Hazardous Materials Toxicology-Clinical Principles of Environmental Health. Baltimore, MD: Williams and Wilkins, 1992. 1091]**PEER REVIEWED**

Controlled exposure effects on volunteers were studied at **toluene** concentrations ranging from 40, 60, or 100 ppm. ... Psychologic measurements indicated decrements in vigilance, visual perception, motor performance, and ability to carry out functions at 100 ppm.
[Sullivan, J.B. Jr., G.R. Krieger (eds.). Hazardous Materials Toxicology-Clinical Principles of Environmental Health. Baltimore, MD: Williams and Wilkins, 1992. 1092]**PEER REVIEWED**

Acute effects in humans following exposure to **toluene**: 50-100 ppm: subjective complaints (fatigue or headache), but probably no observable impairment of reaction time or coordination; 200 ppm: mild throat and eye irritation; 100-300 ppm: detectable signs of incoordination may be expected during exposure periods up to 8 hr; 400 ppm: lacrimation and irritation to the eyes and throat; 300-800 ppm: gross signs of incoordination may be expected during exposure periods up to 8 hr; 1500 ppm: probably not lethal for exposure periods of up to 8 hr; 4000 ppm: would probably cause rapid impairment of reaction time and coordination, exposures of one hr or longer might lead to /CNS depression/ and possibly death; 10,000-30,000 ppm: onset of /CNS depression/ within a few minutes, longer exposures may be lethal. /From table/
[Zenz, C., O.B. Dickerson, E.P. Horvath. Occupational Medicine. 3rd ed. St. Louis, MO., 1994 724]**PEER REVIEWED**

Studies of women exposed to solvents such as benzene, **toluene**, and xylene have shown menstrual disturbances, principally associated with abnormal bleeding.
[Rom, W.N. (ed.). Environmental and Occupational Medicine. 2nd ed. Boston, MA: Little, Brown and Company, 1992. 155]**PEER REVIEWED**

FROM THE STANDPOINT OF CHRONIC EXPOSURE, IT IS CLEAR THAT **TOLUENE** DOES NOT CAUSE THE SEVERE INJURY TO THE BONE MARROW THAT IS CHARACTERISTIC OF BENZENE POISONING.
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Volumes I,II, III. Cincinnati, OH: ACGIH, 1991.

1571]**PEER REVIEWED**

Toluene abuse (to 10,000 ppm) has been linked with kidney disease as evidenced by blood (hematuria), protein (proteinuria), albumin (albuminuria), and pus (pyuria) in the urine, accompanied by elevated serum creatinine, decreased urinary output, and metabolic and renal tubular acidosis.
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Volumes I,II, III. Cincinnati, OH: ACGIH, 1991.
1573]**PEER REVIEWED**

... The highest **toluene** concentrations in air that could be tolerated for 3.5-6 hr without measurable decrements on behavioral test performance were 80 ppm to 100 ppm.
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Volumes I,II, III. Cincinnati, OH: ACGIH, 1991.
1574]**PEER REVIEWED**

The pregnancies of four of five women associated with gross **toluene** abuse (0.5 to 2 cans of spray paint/day for 6 mos to 11 yr) resulted in evidence of renal toxicity (as evidenced by severe renal tubular acidosis), fetal toxicity (manifest as intrauterine growth retardation), and teratogenicity (deformed external ears, ventricular septal defect, micrognathia, hydronephrosis) with facial features reminiscent of the FAS (short palpebral fissures, epicanthal folds, maxillary hypoplasia).
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Volumes I,II, III. Cincinnati, OH: ACGIH, 1991.
1575]**PEER REVIEWED**

In a case study of two adult white males who suffered from **toluene** intoxication while removing glue from tiles in a swimming pool, cardiac arrhythmias were noted. Response seemed to be highly variable among individuals. One person exposed for 2 hr to less than 1890 ppm **toluene** exhibited a rapid heartbeat (sinus tachycardia), while the second person, exposed for 3 hr, exhibited a slow heartbeat (bradycardia).
[Meulenbelt J et al; Br J Ind Med 47: 417-20 (1990) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.31 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

Severe renal tubular acidosis was observed in five pregnant women who were chronic abusers of paints containing **toluene**.
[Goodwin TM; Obstet Gynecol 71: 715-18 (1988) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.36 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

Exposure of students to 75 or 150 ppm **toluene** for 7 hr caused a dose-related impairment of function on digit span, pattern recognition, the one hole test, and pattern memory. There was an effect on the results of the symbol digit test but the effect was not dose related. Subjects served as their own controls. ... There were no differences in the results on simple reaction time, POMS mood scale, visual memory,

hand-eye coordination, Sternberg test, finger tapping, reaction time, continuous performance test, and critical tracking test.
[Echeverria D et al; Br J Ind Med 48: 750-61 (1991) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.40 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

A group of 95-104 workers exposed to TWA of 41-46 ppm **toluene** during shoemaking, printing, and audio equipment production were evaluated for symptoms and signs of exposure when compared to 130 control subjects. The incidence of health-related complaints among the **toluene** exposed workers was two to three times that of the controls. Dizziness was reported by about two-thirds of the **toluene** exposed respondents. These subjects also complained of headaches, sore throats, eye irritation, and difficulty with sleep. When the exposed subjects were divided into two groups, one with TWA exposures of less than 40 ppm and the other with exposures greater than or equal to 40 ppm, the incidence of headache and sore throat, but not dizziness, showed a dose-response pattern.
[Yin S et al; Ind Health 25: 113-30 (1987) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.41 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

Children born to **toluene** abusers have exhibited renal tubular acidosis immediately after birth due to hyperchloremia. In each incident the acidosis was resolved within 3 days of birth.
[Lindemann R; Acta Pediatr Scand 80: 882-4 (1991) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.49 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

Several case series have demonstrated that high exposure to **toluene** through sniffing during pregnancy induces a syndrome that closely resembles the fetal alcohol syndrome, with pre- and postnatal growth deficiency, microcephaly and developmental delay, typical craniofacial features including micrognathia, small palpebral fissures, and ear anomalies.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V71 845 (1999)]**PEER REVIEWED**

Renal tubular acidosis is one of a number of human complications reported in the offspring of mothers inhaling **toluene** during pregnancy. This article reports a case of a premature newborn with renal tubular acidosis probably due to maternal sniffing of paint containing **toluene**. Characteristics of this condition are described as well as its medical management.
[Erramouspe J et al; J Psychoactive Drugs 28 (2): 201-4 (1996)]**PEER REVIEWED**

Skin, Eye and Respiratory Irritations:

A human eye irritant. An experimental skin and severe eye irritant.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996.

3190]**PEER REVIEWED**

Medical Surveillance:

Yearly physical examinations of exposed personnel, with special attention to the eyes and central nervous system, including complete blood count and liver function tests.
[ITII. Toxic and Hazardous Industrial Chemicals Safety Manual. Tokyo, Japan: The International Technical Information Institute, 1988. 526]**PEER REVIEWED**

The clinical examination should include hemocytometric testing and a thrombocyte (platelet) count in view of the possibility that **toluene** may contain a certain proportion of benzene.
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 2185]**PEER REVIEWED**

Hippuric acid levels above 5 g/l of urine may result from exposure greater than 200 ppm determined as a time weighted average.
[Sittig, M. Handbook of Toxic and Hazardous Chemicals and Carcinogens, 1985. 2nd ed. Park Ridge, NJ: Noyes Data Corporation, 1985. 870]**PEER REVIEWED**

Populations at Special Risk:

Preclude individuals from exposure to **toluene** who have central nervous system or liver diseases.
[ITII. Toxic and Hazardous Industrial Chemicals Safety Manual. Tokyo, Japan: The International Technical Information Institute, 1988. 526]**PEER REVIEWED**

Probable Routes of Human Exposure:

NIOSH (NOES Survey 1981-1983) has statistically estimated that 1,625,598 workers (288,299 of these are female) are potentially exposed to **toluene** in the US(1). Occupational exposure to **toluene** may occur through inhalation and dermal contact with this compound at workplaces where **toluene** is produced or used(SRC). The general population may be exposed to **toluene** via inhalation of ambient air, ingestion of food and drinking water, handling of gasoline, and exposure to some consumer products where **toluene** is used as a solvent(SRC).
[(1) NIOSH; National Occupational Exposure Survey (NOES) (1983)]**PEER REVIEWED**

Toluene was detected in hairdresser salons in Norway at concns of 0.04-0.11 mg/cu m(1). The time weighted average (TWA) of **toluene** in the workplace air of a municipal waste composting facility was reported as 188,000 ug/cu m(2). In a 1989 Danish survey on chemical exposures(3), the number of worker exposure events for **toluene** were documented: manufacturing of metals, 420; manufacturing of metal fabricated products 64,000; electrical machinery and apparatus, 1,500; manufacture of transport equipment 2,700; painters and carpenters 15,000; construction workers, 5,400; publishing and printing, 6,300; wholesale trades, 5,000; textile and leather manufacturing, 4,400; wood and furniture manufacturing, 5,900; manufacture of chemicals, 8,700; manufacture of paints and petroleum, 1,400; manufacture of non-metallic mineral products, 2,300; manufacture of optical instruments, 2,500

manufacture of plastic and boat building, 1,100; sewage and refuse disposal, 99; agriculture and forestry, 11,000; health services, 2,600. The total number of work related exposure events was 140,000(3). **Toluene** was detected in the workplace air of glass fiber manufacturing plants and high temperature sealing component and clutch lining plants at a mean concn of 65 ppm(4).
[(1) Hollund BE, Moen BE; Ann Occup Hyg 42: 277-81 (1998) (2) Eitzer BD; Environ Sci Technol 29: 896-902 (1995) (3) Brandorff NP et al; Occup Environ Med 52: 454-63 (1995) (4) Angerer J, Kraemer A; Int Arch Occup Environ Health 69: 91-96 (1997)]**PEER REVIEWED**

Body Burden:

Toluene was identified, not quantified, in 8 samples of mothers' milk from 4 urban areas(1). **Toluene** was detected in 250 of 250 specimens of human blood at concns of 0.2-38 ppb (1.5 ppb avg)(2). **Toluene** was detected in 91% of the samples of the National Human Adipose Tissue Survey at a max concn of 250 ppb(3). **Toluene** was identified, not quantified, in expired breath of people at service stations during fueling(4). The mean concn of **toluene** in the blood of non-occupationally exposed individuals in the US was 0.52 ppb(5). The avg concn of **toluene** in the blood and urine of workers in glass fiber and clutch lining plants were 911 ug/l and 2.9 mg/l, respectively(6).
[(1) Pellizzari ED et al; Bull Environ Contam Toxicol 28: 322-8 (1982) (2) Antoine SR et al; Bull Environ Contam Toxicol 36: 364-71 (1986) (3) Stanley JS; Broad Scan Analysis of the FY82 National Human Adipose Tissue Survey Specimens Vol. I Executive Summary p. 5 USEPA-560/5-86-035 (1986) (4) Lindstrom AB, Pleil J; J Air Waste Manage Assoc 46: 676-82 (1996) (5) Ashley DL et al; Clin Chem 40: 1401-14 (1994) (6) Angerer J, Kraemer A; Int Arch Occup Environ Health 69: 91-96 (1997)]**PEER REVIEWED**

Average Daily Intake:

AIR INTAKE (assume median concn 11 ppb(1)) 843 ug; WATER INTAKE (assume 2 ppb(2)) 4 ug; FOOD INTAKE - insufficient data.
[(1) Brodzinsky R, Singh HB; Volatile Organics in the Atmosphere and Assessment of available data: p. 126-7 SRI Contract 68-02-3459 (1982) (2) Otson R et al; J Assoc Off Analyt Chem 65: 1370-4 (1982)]**PEER REVIEWED**

Minimum Fatal Dose Level:

Ingestion of approximately 60 ml (625 mg/kg) of **toluene** proved fatal for a while male mental patient.
[Ameno K et al; Forensic Sci Int 41: 255-60 (1989) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.52 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

TOLUENE

CASRN: 108-88-3

For other data, click on the Table of Contents

Evidence for Carcinogenicity:

Evaluation: There is inadequate evidence for the carcinogenicity of **toluene** in humans. There is evidence suggesting lack of carcinogenicity of **toluene** in experimental animals. Overall evaluation: **Toluene** is not classifiable as to its carcinogenicity to humans (Group 3).
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V71 855 (1999)]**PEER REVIEWED**

CLASSIFICATION: D; not classifiable as to human carcinogenicity. BASIS FOR CLASSIFICATION: No human data and inadequate animal data. **Toluene** did not produce positive results in the majority of genotoxic assays. HUMAN CARCINOGENICITY DATA: None.
[U.S. Environmental Protection Agency's Integrated Risk Information System (IRIS) on Toluene (108-88-3) Available from: http://www.epa.gov/ngispgm3/iris on the Substance File List as of March 15, 2000]**PEER REVIEWED**

A4. A4= Not classifiable as a human carcinogen.
[American Conference of Governmental Industrial Hygienists. TLVs and BEIs. Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. Cincinnati, OH. 2000. 67]**QC REVIEWED**

TOLUENE

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Human Toxicity Excerpts:

Among 61 painters inhaling 100-1100 ppm **toluene** for 2 wk to 5 yr, depressed erythrocyte counts with elevated hemoglobin, mean corpuscular volumes, and elevated mean corpuscular hemoglobin were found in 5% to 30% compared with groups of 73-395 workers not known to be exposed to **toluene**; differential leukocyte counts were not significantly different between the **toluene**-exposed and the reference workers.
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Volumes I,II, III. Cincinnati, OH: ACGIH, 1991. 1573]**PEER REVIEWED**

... **TOLUENE** CAUSES DEFATTING OF SKIN WITH SUBSEQUENT DANGER OF DRYNESS, FISSURING AND SECONDARY INFECTION.
[International Labour Office. Encyclopedia of Occupational Health and Safety. Volumes I and II. New York: McGraw-Hill Book Co., 1971. 1414]**PEER REVIEWED**

... SUDDEN DEATH AMONG "SNIFFERS" MAY BE ATTRIBUTED TO LETHAL CARDIAC ARRHYTHMIAS FOLLOWING SENSITIZATION OF THE MYOCARDIUM.
[Hamilton, A., and H. L. Hardy. Industrial Toxicology. 3rd ed. Acton, Mass.: Publishing Sciences Group, Inc., 1974. 276]**PEER REVIEWED**

... PERMANENT ENCEPHALOPATHY ... /IN/ MAN WHO INHALED **TOLUENE** REGULARLY FOR OVER 14 YR /WAS DESCRIBED/.
[American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices. 5th ed. Cincinnati, OH:American Conference of Governmental Industrial Hygienists, 1986. 578]**PEER REVIEWED**

VAPORS OF **TOLUENE** CAUSE NOTICEABLE SENSATION OF IRRITATION TO HUMAN EYES AT 300-400 PPM IN AIR, BUT EVEN AT 800 PPM IRRITATION IS SLIGHT. ... IN HUMAN VOLUNTEERS EXPOSED TO CONCN AS HIGH AS 800 PPM ... DILATION OF PUPILS & IMPAIRMENT OF REACTION IN ASSOCIATION WITH FATIGUE AT END OF 8 HR, ALSO SLIGHT PALLOR OF FUNDI.
[Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986. 927]**PEER REVIEWED**

Metabolic acidosis with a high "anion gap" in 2 patients who had been sniffing **toluene**.
[Reynolds, J.E.F., Prasad, A.B. (eds.) Martindale-The Extra Pharmacopoeia. 28th ed. London: The Pharmaceutical Press, 1982. 1455]**PEER REVIEWED**

A report of 2 children who sniffed glue containing **toluene**. One of the children became comatose after

an episode of "sniffing" which lasted for several hours. Adverse effects included reduced appetite, nightmares, vertical nystagmus, and incoordination.
[Reynolds, J.E.F., Prasad, A.B. (eds.) Martindale-The Extra Pharmacopoeia. 28th ed. London: The Pharmaceutical Press, 1982. 1455]**PEER REVIEWED**

WORKERS IN PHARMACEUTICAL PLANT IN FRANCE EXPOSED TO **TOLUENE** DEVELOPED LEUKOPENIA, & NEUTROPENIA. WITHIN 6 MO, THOSE AFFECTED SHOWED INCR IN CLOTTING TIME & DECR IN PROTHROMBIN LEVEL ...
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1329]**PEER REVIEWED**

PERIPHERAL BLOOD LYMPHOCYTES FROM 32 MALE ROTOGRAVURE WORKERS SHOWED NO SIGNIFICANT DIFFERENCE FROM CONTROLS IN FREQUENCY OF CHROMOSOME ABERRATIONS & SISTER CHROMATID EXCHANGES.
[MAKI-PAAKKANEN J ET AL; J TOXICOL ENVIRON HEALTH 6: 775 (1980)]**PEER REVIEWED**

Patients (3) with history of recurrent **toluene** abuse were hospitalized and severe metabolic acidosis, electrolyte abnormalities, hypoalkemia, and muscular weakness were present. Distal renal tubular acidosis was believed to be present in 2/3 patients.
[Fiscman CM, Oster JR; Am Med Assoc 241 (16): 1713-15 (1979) as cited in NRC; Alkyl Benzenes p.284 (1981)]**PEER REVIEWED**

Child of a mother with a 14 year history of solvent abuse showed symptoms of fetal alcohol syndrome.
[Toutant C, Lippman S; Lancet 1 (8130): 1356 (1979)]**PEER REVIEWED**

A 27-year-old male developed cerebral and cerebellar atrophy over a period of five years of extensive glue sniffing. He also developed bilateral optic atrophy with blindness and severe sensorineural hearing loss.
[Ehyai A, Freemon FR; J Neural Neurosurg Psychiatry 46 (4): 349-51 (1983)]**PEER REVIEWED**

Toluene appears to produce reversible effects upon liver, renal, and nervous systems. ... The nervous system appears to be the most sensitive to the effects of **toluene**. ... High level **toluene** exposures produced incoordination, ataxia, unconsciousness and eventually, death. Lower level acute exposures in man produce dizziness, exhilaration and confusion. Activity level has been inadequately studied. Schedule controlled behaviors have been reported to produce inverted U-shaped concentration-effect curves on response rate measures. Alterations at levels as low as 150 ppm have been reported when appetitive contingencies are used. Very few studies of the nervous system have been performed at levels below 1000 ppm and most of the results were inconclusive. ...
[Benignus VA; Neurobehav Toxicol Teratol 3 (4): 407-15 (1981)]**PEER REVIEWED**

Lethal levels 1.0 mg%; 10.0 ug/ml
[Winek, C.L. Drug and Chemical Blood-Level Data 1985. Pittsburgh, PA: Allied Fischer Scientific, 1985.]**PEER REVIEWED**

IN EXPERIMENTS IN VITRO, **TOLUENE** DID NOT CHANGE NUMBER OF SISTER-CHROMATID EXCHANGES OR THE NUMBER OF CHROMOSOMAL ABERRATIONS IN HUMAN LYMPHOCYTES.
[GERNER-SCMIDT P, FRIEDRICH U; MUTATION RESEARCH 58: 313 (1978)]**PEER REVIEWED**

A 28 yr old painter who was believed to be a habitual **toluene** sniffer was admitted to Chiba Emergency Medical Center on several occasions. Symptoms included: Tremors of the upper extremeties, staggering of gait, slurred speech, slight mental deterioration, pendular nystagmus, bradycardia, mild tremor of the leg, action myoclonus, and head and trunchal titubation. There was no dysmetria. The involuntary movements were classified as hyperkinesie volitionnelle. Muscle tone was hypotonic. Muscle weakness and atrophy were not seen. Deep tendon reflexes were all exaggerated, but there was no pathological reflex. He showed wide-based ataxic gait. Sensory and autonomic functions were normal. Blood, urine and cerebrospinal fluid analysis appeared normal. Electroencephalography showed 40-50 uV, 9-10 c/s alpha waves with a few fast waves. Brain CT scan revealed a moderate enlargement of the lateral and third ventricles. Surface electromyography was performed on the proximal musculature of the arm. 3 c/s reciprocal rhythmical grouping discharges were found at the terminal phase of the elbow bending. The tremor was diminished by 20 minutes ischemic compression test of the arm. With respect to therapy, clonazepam was useful for hyperkinesie volitionnelle. He became able to drink a cup of water without spilling it by his own hands, and was discharged from hospital on April 3rd, 1981. It was believed that he was a habitual sniffer to **toluene**. On June 30th, 1983 he was found comatose. On admission to Chiba Emergency Medical Center, his breath smelt of **toluene**. His blood **toluene** level was 7.53 ppm, and urinary hippuric acid concentration was 9,500 mg/l. He died on July 9th, 1983, because of disseminated intravascular coagulation, multiple organ failure and perforation of the terminal ileum. Autopsy was performed and neuropathological findings were as follows. 1) Diffuse demyelination and gliosis of the cerebral and cerebella white matter. 2) Marked loss of Purkinje cells of the cerebellum. 3) Astrocytic proliferation of the dentate fugal system and inferior olivary nucleus of medulla. ...
[Arai K et al; Brain Nerve Tokyo 38 (12): 1181-86 (1986)]**PEER REVIEWED**

Autopsy findings on a man who fell from a height due to acute **toluene** poisoning while painting are described. Gas chromatographic examination revealed that the **toluene** concentrations of his blood, lung, liver and brain were 48, 35, 65 and 80 ug/g, respectively. These **toluene** levels were not enough to be definitely lethal, but were enough to anesthetize the central nervous system.
[Takeichi S et al; Forensic Sci Int 32 (2): 109-16 (1986)]**PEER REVIEWED**

The psychological performance of 43 rotogravure printers exposed to a mean time- weighted average of 117 ppm **toluene** for a mean time period of 21.7 yr was compared to that of 31 offset printers with a mean working period of 23 yr. The offset printers were exposed to mixtures of aliphatic hydrocarbons or ethyl acetate (amounts not given) for a total of 10 to 60 min daily. Drinking habits were considered in grouping the workers. The test battery consisted of standardized tests for verbal and visual cognition and memory, perceptual motor speed, and psychomotor abilities. Performances of the two printer groups were similar with rotogravure printers having statistically significant lower scores on tests measuring visual cognitive abilities. Mean test performances indicated that drinking habits did not explain the impairment of visual cognitive abilities.
[Hanninen H et al; Int Arch Occupat Environ Health 59 (5): 475-83

(1987)]**PEER REVIEWED**

Acute poisoning may result from exposure to high concn of **toluene**; A /CNS depressant/ effect is produced. Human death has resulted from exposure to 10,000 ppm. **Toluene** is more acutely toxic than benzene; however, severe blood disorders of the type associated with benzene are not reported. Inhalation of 200 ppm has affected the CNS in humans.
[Cleland, J.G., G.L. Kingsbury. Multimedia Environmental Goals for Environmental Assessment. Volume 1. EPA-600/7-77-136a. Research Triangle Park, NC: EPA, Nov. 1977.,p. E-146]**PEER REVIEWED**

Vapors irritate eyes and upper respiratory tract; Cause dizziness, headache, anesthesia, and respiratory arrest. Liquid irritates eyes. If aspirated, causes coughing, gagging, distress, and rapidly developing pulmonary edema. If ingested causes vomiting, griping, diarrhea, and depressed respiration. Kidney and liver damage may follow ingestion.
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

In recent years some youngsters have been indulging in what is called thinner inhalation, posing a serious social problem. Organic solvents have also been widely used industrially as adhesives or degreasing and rinsing agents, generating a kind of occupational disease which has become a medical problem. Some school children who refuse to go to school complaining of headache, head heaviness, blurred vision, diplopia, or dizziness, may actually have **toluene** toxicosis caused by the adhesive they use in constructing plastic models. /An examination of/ 35 such patients neurogically, found some impairment in the cerebellar cortex, cerebellar nuclei, or efferent pathways. This report is presented to invite comments from other researchers.
[Sakata E et al; Pract Otal Kyoto 79 (12): 1999-2013 (1986)]**PEER REVIEWED**

Severe, acute **toluene** intoxication in two workers was described. Special attention was paid to the metabolism of **toluene** in man and to the choice of reference parameters to monitor intoxication. The men had tiled a small swimming pool to be used for exercise programs in a rehabilitation clinic. They had used a special glue to make the joints of cement between the tiles resistant to bleaching solution; the next day they removed the excess glue using **toluene**. One worker was exposed for 2 hours and the other for 3 hours. Both were overcome with the fumes, and were found lying at the bottom of the pool. Symptoms included stupefaction, paresis, and amnesia. Patient-A had mucosal irritation of the eyes and slurred speech. He was stuporose and unable to walk or sit. His amnesia lasted for about 3 hours. Patient-B had mucosal irritation of the eyes, was drowsy, and was just able to walk. He had normal speech and complained of headache. The duration of his amnesia was about 2.5 hours. Solid evidence for **toluene** exposure was provided by the blood **toluene** concentration. The concentration 2 hours after exposure was 4.1 mg/l in patient-A and 2.2 mg/l in patient-B.
[Meulenbelt J et al; Br J Ind Med 47 (6): 417-20 (1990)]**PEER REVIEWED**

The memory sequelae for a group of female workers accidentally exposed to organic solvents were examined retrospectively to evaluate complaints of residual memory impairment. The subjects included seven employees (mean age 32.1 years) who agreed to retesting and who had been severely intoxicated

by exposure to **toluene** and aliphatic hydrocarbons found in adhesives used in the manufacture of tennis balls. They were compared to eight workers (mean age 33.7 years) who were solvent exposed but not affected by the accident and ten workers (mean age 36.6 years) who had no exposure. Acute symptoms included faintness, nausea, vomiting, and headache. Complaints of impaired memory, personality changes, and loss of confidence persisted 8 months after exposure. Memory testing was first performed 2 months after exposure, with the follow up 6 months later to assess recovery. The three memory tasks included paired associate task, serial position task, and Brown-Peterson task. The subjects showed normal patterns of performance on tests of learning and short term and long term memory, but demonstrated marked difficulties when attention had to be divided between two resource competing tasks. The clearest evidence of impairment was observed in the Brown-Peterson task, where the acute group showed a significantly greater increase in word recall omission after periods of counting backwards in threes. The magnitude of the memory sequelae was not correlated with scores of self rated depression. It was concluded that solvent intoxication can cause neuropsychological sequelae lasting more than 8 months; memory tasks could prove useful in identifying memory impairment in other occupationally exposed groups.
[Stollery BT, Flindt MLH; Scand J Work, Environ, Health 14 (1): 45-8 (1988)]**PEER REVIEWED**

In a cross-sectional study of 181 male workers of a rotogravure printing plant, most of whom were exposed to **toluene** levels well above the GDR threshold limit values, 55 subjects revealed pathological liver screening values (activities of serum aspartate aminotransferase, alanine aminotransferase, gamma glutamyltransferase; liver size). The differential diagnostic examination showed in 51 of these 55 subjects an association with competing factors such as alcohol abuse (78%) and overweight (40%), to a slight extent disorders of fat and carbohydrate metabolism and of the gallbladder. Drug intake did not play any role. The variance and regression analyses of the biochemical data have shown that alcohol significantly and considerably increases the activities of all three enzymes tested. Bodyweight had a similar, but less pronounced, significant effect. On the other hand, in subjects with a higher alcohol intake the activities of liver enzymes in highly **toluene** exposed subgroups were significantly and clearly lower than among slightly **toluene** exposed workers.
[Boewer C et al; Int Arch Occup Environ Health 60 (3): 181-6 (1988)]**PEER REVIEWED**

General health effects include lethality, growth, morbidity, liver and kidney damage and miscellaneous effects. Neurobehavioral effects include epidemiological and clinical findings, activity and sleep, performance and learning, electrophysiological effects. Evaluation and synthesis of data is included. It was concluded that low level exposure to **toluene** has its primary effect on the CNS. From a systematic or general point of view it is not clear what this effect is. Both depressant and excitatory effects (possibly concentration dependent) were reported as well as other kinds of results. Other health effects were not life threatening at any exposure level short of that producing lethality. Effects were reversible even at extremely high exposure levels for very long durations.
[Benignus VA; Neurotoxicol 2 (3): 567-88 (1981)]**PEER REVIEWED**

Toluene embryopathy is characterized by microcephaly, central nervous system dysfunction, attentional deficits and hyperactivity, developmental delay with greater language deficits, minor craniofacial and limb anomalies, and variable growth deficiency. Previously, three affected children, born to women who inhaled **toluene** regularly throughout pregnancy, have been reported. Two more cases are described emphasizing the importance of **toluene** as a potential human teratogen.

[Hersh JH; J Med Genet 26 (5): 333-7 (1989)]**PEER REVIEWED**

Neurobehavioral tests were undertaken by 30 female workers exposed to **toluene** and matched controls with low occupational exposure to **toluene**. The environmental air levels (TWA) of **toluene** was 88 ppm for the exposed workers and 13 ppm for the controls. The **toluene** in blood concentrations for the exposed workers was 1.25 mg/l and for the controls 0.16 mg/l. Statistically significant differences between workers exposed to **toluene** and controls in neurobehavioral tests measuring manual dexterity (grooved peg board), a visual scanning (trail making, visual reproduction, Benton visual retention, and digit symbol), and verbal memory (digit span) were observed. Further, the performance at each of these tests was related to time weighted average exposure concentrations of air **toluene**. The workers exposed to **toluene** had no clinical symptoms or signs. The question arises as to whether these impairments in neurobehavioral tests are reversible or whether they could be a forerunner of more severe damage.
[Foo SC et al; BR J Ind Med 47 (7): 480-4 (1990)]**PEER REVIEWED**

When compared with benzene, **toluene** has little to no effect on immunocompetence. However, it should be noted that **toluene** exposure effectively attenuates the immunotoxic effects of benzene (probably because of competition for metabolic enzymes).
[Klaassen, C.D., M.O. Amdur, Doull J. (eds.). Casarett and Doull's Toxicology. The Basic Science of Poisons. 5th ed. New York, NY: McGraw-Hill, 1995. 380]**PEER REVIEWED**

Neutral organic solvents such as ... **toluene** ... cause pain on contacting the eye, and examination after a generous splash of solvent shows dulling of the cornea. The epithelium will show punctate staining with fluorescein. The damage appears to be scattered loss of epithelial cells due to solution of some of the fats that occur in these cells.
[Klaassen, C.D., M.O. Amdur, Doull J. (eds.). Casarett and Doull's Toxicology. The Basic Science of Poisons. 5th ed. New York, NY: McGraw-Hill, 1995. 586]**PEER REVIEWED**

Toxicities associated with **toluene**: CNS depression, syncope, coma, cardiac arrhythmias and sudden death, ataxia, convulsions, rhabdomyolysis, increased creatine phosphokinase, abdominal pain, nausea, vomiting, hematemesis, peripheral neuropathy, paresthesias, encephalopathy, optic neuropathy, cerebella ataxia, distal renal tubular acidosis, hyperchloremia, hypokalemia, azotemia, hypophosphatemia, hematuria, proteinuria, pyruria, normalities, decreased cognitive function, fatal overdose. /From table/
[Ellenhorn, M.J., S. Schonwald, G. Ordog, J. Wasserberger. Ellenhorn's Medical Toxicology: Diagnosis and Treatment of Human Poisoning. 2nd ed. Baltimore, MD: Williams and Wilkins, 1997. 1494]**PEER REVIEWED**

Women workers exposed to high air concentrations of **toluene** (50-150 ppm) appeared to have a higher incidence of spontaneous abortion than a similar group of women with no occupational exposure to **toluene**.
[Ellenhorn, M.J., S. Schonwald, G. Ordog, J. Wasserberger. Ellenhorn's Medical Toxicology: Diagnosis and Treatment of Human Poisoning. 2nd ed. Baltimore, MD: Williams and Wilkins, 1997. 166]**PEER REVIEWED**

Maternal spray paint or glue sniffing leads to maternal complications including renal tubular acidosis, hypokalemia, hypocalcemia, cardiac arrhythmias, rhabdomyolysis, and premature labor. Premature **toluene** exposure leads to a characteristic pattern of anomalies similar to findings in infants exposed to

alcohol in utero, consisting of an increased incidence of malformations, poor growth, and developmental delays.
[Ellenhorn, M.J., S. Schonwald, G. Ordog, J. Wasserberger. Ellenhorn's Medical Toxicology: Diagnosis and Treatment of Human Poisoning. 2nd ed. Baltimore, MD: Williams and Wilkins, 1997. 166]**PEER REVIEWED**

Eye and upper airway irritation occurred after a 6.5 hr exposure to an air level of 100 ppm (377 mg/cu m) **toluene**, and lachrymation was seen at 500 mg/cu m.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47 101 (1989)]**PEER REVIEWED**

Volunteers exposed to 100 ppm (377 mg/cu m) **toluene** for 6 hr/day for four days suffered from subjective complaints of headache, dizziness and a sensation of intoxication. In subjects exposed to 750 mg/cu m for 8 hr, fatigue, muscular weakness, confusion, impaired coordination, enlarged pupils and accommodation disturbances were experienced; at about 3000 mg/cu m, severe fatigue, pronounced nausea, mental confusion, considerable incoordination with staggering gait and strongly affected pupillary light reflexes were observed. After exposure at the high level, muscular fatigue, nervousness and insomnia lasted for several days. Heavy accidental exposure leads to coma.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47 101 (1989)]**PEER REVIEWED**

Humans exposed to concentrations of **toluene** of between 200-800 ppm may experience respiratory and ocular irritation.
[Sullivan, J.B. Jr., G.R. Krieger (eds.). Hazardous Materials Toxicology-Clinical Principles of Environmental Health. Baltimore, MD: Williams and Wilkins, 1992. 1090]**PEER REVIEWED**

Children with microcephaly, minor craniofacial and limb anomalies, central nervous system defects, attention disorders, developmental delay, learning disorders, and language deficits were born to mothers who abuse **toluene** by inhalation during pregnancy.
[Sullivan, J.B. Jr., G.R. Krieger (eds.). Hazardous Materials Toxicology-Clinical Principles of Environmental Health. Baltimore, MD: Williams and Wilkins, 1992. 1091]**PEER REVIEWED**

Controlled exposure effects on volunteers were studied at **toluene** concentrations ranging from 40, 60, or 100 ppm. ... Psychologic measurements indicated decrements in vigilance, visual perception, motor performance, and ability to carry out functions at 100 ppm.
[Sullivan, J.B. Jr., G.R. Krieger (eds.). Hazardous Materials Toxicology-Clinical Principles of Environmental Health. Baltimore, MD: Williams and Wilkins, 1992. 1092]**PEER REVIEWED**

Acute effects in humans following exposure to **toluene**: 50-100 ppm: subjective complaints (fatigue or headache), but probably no observable impairment of reaction time or coordination; 200 ppm: mild throat and eye irritation; 100-300 ppm: detectable signs of incoordination may be expected during

exposure periods up to 8 hr; 400 ppm: lacrimation and irritation to the eyes and throat; 300-800 ppm: gross signs of incoordination may be expected during exposure periods up to 8 hr; 1500 ppm: probably not lethal for exposure periods of up to 8 hr; 4000 ppm: would probably cause rapid impairment of reaction time and coordination, exposures of one hr or longer might lead to /CNS depression/ and possibly death; 10,000-30,000 ppm: onset of /CNS depression/ within a few minutes, longer exposures may be lethal. /From table/
[Zenz, C., O.B. Dickerson, E.P. Horvath. Occupational Medicine. 3rd ed. St. Louis, MO., 1994 724]**PEER REVIEWED**

Studies of women exposed to solvents such as benzene, **toluene**, and xylene have shown menstrual disturbances, principally associated with abnormal bleeding.
[Rom, W.N. (ed.). Environmental and Occupational Medicine. 2nd ed. Boston, MA: Little, Brown and Company, 1992. 155]**PEER REVIEWED**

FROM THE STANDPOINT OF CHRONIC EXPOSURE, IT IS CLEAR THAT **TOLUENE** DOES NOT CAUSE THE SEVERE INJURY TO THE BONE MARROW THAT IS CHARACTERISTIC OF BENZENE POISONING.
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Volumes I,II, III. Cincinnati, OH: ACGIH, 1991. 1571]**PEER REVIEWED**

Toluene abuse (to 10,000 ppm) has been linked with kidney disease as evidenced by blood (hematuria), protein (proteinuria), albumin (albuminuria), and pus (pyuria) in the urine, accompanied by elevated serum creatinine, decreased urinary output, and metabolic and renal tubular acidosis.
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Volumes I,II, III. Cincinnati, OH: ACGIH, 1991. 1573]**PEER REVIEWED**

... The highest **toluene** concentrations in air that could be tolerated for 3.5-6 hr without measurable decrements on behavioral test performance were 80 ppm to 100 ppm.
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Volumes I,II, III. Cincinnati, OH: ACGIH, 1991. 1574]**PEER REVIEWED**

The pregnancies of four of five women associated with gross **toluene** abuse (0.5 to 2 cans of spray paint/day for 6 mos to 11 yr) resulted in evidence of renal toxicity (as evidenced by severe renal tubular acidosis), fetal toxicity (manifest as intrauterine growth retardation), and teratogenicity (deformed external ears, ventricular septal defect, micrognathia, hydronephrosis) with facial features reminiscent of the FAS (short palpebral fissures, epicanthal folds, maxillary hypoplasia).
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Volumes I,II, III. Cincinnati, OH: ACGIH, 1991. 1575]**PEER REVIEWED**

In a case study of two adult white males who suffered from **toluene** intoxication while removing glue

from tiles in a swimming pool, cardiac arrhythmias were noted. Response seemed to be highly variable among individuals. One person exposed for 2 hr to less than 1890 ppm **toluene** exhibited a rapid heartbeat (sinus tachycardia), while the second person, exposed for 3 hr, exhibited a slow heartbeat (bradycardia).
[Meulenbelt J et al; Br J Ind Med 47: 417-20 (1990) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.31 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

Severe renal tubular acidosis was observed in five pregnant women who were chronic abusers of paints containing **toluene**.
[Goodwin TM; Obstet Gynecol 71: 715-18 (1988) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.36 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

Exposure of students to 75 or 150 ppm **toluene** for 7 hr caused a dose-related impairment of function on digit span, pattern recognition, the one hole test, and pattern memory. There was an effect on the results of the symbol digit test but the effect was not dose related. Subjects served as their own controls. ... There were no differences in the results on simple reaction time, POMS mood scale, visual memory, hand-eye coordination, Sternberg test, finger tapping, reaction time, continuous performance test, and critical tracking test.
[Echeverria D et al; Br J Ind Med 48: 750-61 (1991) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.40 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

A group of 95-104 workers exposed to TWA of 41-46 ppm **toluene** during shoemaking, printing, and audio equipment production were evaluated for symptoms and signs of exposure when compared to 130 control subjects. The incidence of health-related complaints among the **toluene** exposed workers was two to three times that of the controls. Dizziness was reported by about two-thirds of the **toluene** exposed respondents. These subjects also complained of headaches, sore throats, eye irritation, and difficulty with sleep. When the exposed subjects were divided into two groups, one with TWA exposures of less than 40 ppm and the other with exposures greater than or equal to 40 ppm, the incidence of headache and sore throat, but not dizziness, showed a dose-response pattern.
[Yin S et al; Ind Health 25: 113-30 (1987) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.41 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

Children born to **toluene** abusers have exhibited renal tubular acidosis immediately after birth due to hyperchloremia. In each incident the acidosis was resolved within 3 days of birth.
[Lindemann R; Acta Pediatr Scand 80: 882-4 (1991) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.49 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

Several case series have demonstrated that high exposure to **toluene** through sniffing during pregnancy induces a syndrome that closely resembles the fetal alcohol syndrome, with pre- and postnatal growth deficiency, microcephaly and developmental delay, typical craniofacial features including micrognathia, small palpebral fissures, and ear anomalies.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V71 845 (1999)]**PEER REVIEWED**

Renal tubular acidosis is one of a number of human complications reported in the offspring of mothers inhaling **toluene** during pregnancy. This article reports a case of a premature newborn with renal tubular acidosis probably due to maternal sniffing of paint containing **toluene**. Characteristics of this condition are described as well as its medical management.
[Erramouspe J et al; J Psychoactive Drugs 28 (2): 201-4 (1996)]**PEER REVIEWED**

TOLUENE

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Skin, Eye and Respiratory Irritations:

A human eye irritant. An experimental skin and severe eye irritant.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 3190]**PEER REVIEWED**

TOLUENE

CASRN: 108-88-3

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Medical Surveillance:

Yearly physical examinations of exposed personnel, with special attention to the eyes and central nervous system, including complete blood count and liver function tests.
[ITII. Toxic and Hazardous Industrial Chemicals Safety Manual. Tokyo, Japan: The International Technical Information Institute, 1988. 526]**PEER REVIEWED**

The clinical examination should include hemocytometric testing and a thrombocyte (platelet) count in view of the possibility that **toluene** may contain a certain proportion of benzene.
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 2185]**PEER REVIEWED**

Hippuric acid levels above 5 g/l of urine may result from exposure greater than 200 ppm determined as a time weighted average.
[Sittig, M. Handbook of Toxic and Hazardous Chemicals and Carcinogens, 1985. 2nd ed. Park Ridge, NJ: Noyes Data Corporation, 1985. 870]**PEER REVIEWED**

TOLUENE

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Populations at Special Risk:

Preclude individuals from exposure to **toluene** who have central nervous system or liver diseases.
[ITII. Toxic and Hazardous Industrial Chemicals Safety Manual. Tokyo, Japan: The International Technical Information Institute, 1988. 526]**PEER REVIEWED**

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Probable Routes of Human Exposure:

NIOSH (NOES Survey 1981-1983) has statistically estimated that 1,625,598 workers (288,299 of these are female) are potentially exposed to **toluene** in the US(1). Occupational exposure to **toluene** may occur through inhalation and dermal contact with this compound at workplaces where **toluene** is produced or used(SRC). The general population may be exposed to **toluene** via inhalation of ambient air, ingestion of food and drinking water, handling of gasoline, and exposure to some consumer products where **toluene** is used as a solvent(SRC).

[(1) NIOSH; National Occupational Exposure Survey (NOES) (1983)]**PEER REVIEWED**

Toluene was detected in hairdresser salons in Norway at concns of 0.04-0.11 mg/cu m(1). The time weighted average (TWA) of **toluene** in the workplace air of a municipal waste composting facility was reported as 188,000 ug/cu m(2). In a 1989 Danish survey on chemical exposures(3), the number of worker exposure events for **toluene** were documented: manufacturing of metals, 420; manufacturing of metal fabricated products 64,000; electrical machinery and apparatus, 1,500; manufacture of transport equipment 2,700; painters and carpenters 15,000; construction workers, 5,400; publishing and printing, 6,300; wholesale trades, 5,000; textile and leather manufacturing, 4,400; wood and furniture manufacturing, 5,900; manufacture of chemicals, 8,700; manufacture of paints and petroleum, 1,400; manufacture of non-metallic mineral products, 2,300; manufacture of optical instruments, 2,500 manufacture of plastic and boat building, 1,100; sewage and refuse disposal, 99; agriculture and forestry, 11,000; health services, 2,600. The total number of work related exposure events was 140,000(3). **Toluene** was detected in the workplace air of glass fiber manufacturing plants and high temperature sealing component and clutch lining plants at a mean concn of 65 ppm(4).

[(1) Hollund BE, Moen BE; Ann Occup Hyg 42: 277-81 (1998) (2) Eitzer BD; Environ Sci Technol 29: 896-902 (1995) (3) Brandorff NP et al; Occup Environ Med 52: 454-63 (1995) (4) Angerer J, Kraemer A; Int Arch Occup Environ Health 69: 91-96 (1997)]**PEER REVIEWED**

TOLUENE

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For other data, click on the Table of Contents

Body Burden:

Toluene was identified, not quantified, in 8 samples of mothers' milk from 4 urban areas(1). **Toluene** was detected in 250 of 250 specimens of human blood at concns of 0.2-38 ppb (1.5 ppb avg)(2). **Toluene** was detected in 91% of the samples of the National Human Adipose Tissue Survey at a max concn of 250 ppb(3). **Toluene** was identified, not quantified, in expired breath of people at service stations during fueling(4). The mean concn of **toluene** in the blood of non-occupationally exposed individuals in the US was 0.52 ppb(5). The avg concn of **toluene** in the blood and urine of workers in glass fiber and clutch lining plants were 911 ug/l and 2.9 mg/l, respectively(6).

[(1) Pellizzari ED et al; Bull Environ Contam Toxicol 28: 322-8 (1982) (2) Antoine SR et al; Bull Environ Contam Toxicol 36: 364-71 (1986) (3) Stanley JS; Broad Scan Analysis of the FY82 National Human Adipose Tissue Survey Specimens Vol. I Executive Summary p. 5 USEPA-560/5-86-035 (1986) (4) Lindstrom AB, Pleil J; J Air Waste Manage Assoc 46: 676-82 (1996) (5) Ashley DL et al; Clin Chem 40: 1401-14 (1994) (6) Angerer J, Kraemer A; Int Arch Occup Environ Health 69: 91-96 (1997)]**PEER REVIEWED**

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Average Daily Intake:

AIR INTAKE (assume median concn 11 ppb(1)) 843 ug; WATER INTAKE (assume 2 ppb(2)) 4 ug; FOOD INTAKE - insufficient data.

[(1) Brodzinsky R, Singh HB; Volatile Organics in the Atmosphere and Assessment of available data: p. 126-7 SRI Contract 68-02-3459 (1982) (2) Otson R et al; J Assoc Off Analyt Chem 65: 1370-4 (1982)]**PEER REVIEWED**

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For other data, click on the Table of Contents

Minimum Fatal Dose Level:

Ingestion of approximately 60 ml (625 mg/kg) of **toluene** proved fatal for a while male mental patient. [Ameno K et al; Forensic Sci Int 41: 255-60 (1989) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.52 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

TOLUENE

CASRN: 108-88-3

For other data, click on the Table of Contents

Emergency Medical Treatment:

Emergency Medical Treatment:

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The following Overview, *** **TOLUENE** ***, is relevant for this HSDB record chemical.

Life Support:

```
o   This overview assumes that basic life support measures
    have been instituted.
```

Clinical Effects:

```
SUMMARY OF EXPOSURE
 0.2.1.1 ACUTE EXPOSURE
   o   ACUTE INGESTION -
    1.  Causes CNS depression, oropharyngeal and gastric pain,
        vomiting.
   o   ACUTE INHALATION -
    1.  Causes CNS excitation followed by CNS depression and
        nausea.  Ataxia, fatigue, seizures and general
        anesthesia occur at high concentrations.
   o   CHRONIC INHALATION -
    1.  SYNDROMES - Muscular weakness, gastroenteritis, renal
        tubular acidosis, and neuropsychiatric syndrome are
        common in toluene sniffers.
    2.  EFFECTS - may include hypokalemia, hematuria,
        proteinuria, oliguria, paresis, rhabdomyolysis,
        hallucinations, hyperactive reflexes, peripheral
        neuropathy, personality changes, tremors, headaches,
        emotional lability, memory loss.
    3.  SEQUELAE - Progressive, irreversible encephalopathy
        with cognitive difficulty and cerebellar ataxia, and
        organic affective syndromes have been described.
   o   EYE EXPOSURE -
    1.  Blepharospasm, conjunctivitis, corneal edema, and
```

corneal abrasions usually resolve over 1-2 days.

- DERMAL EXPOSURE -

1. Prolonged or repeated dermal exposure to the liquid may defat the skin.

VITAL SIGNS

0.2.3.1 ACUTE EXPOSURE

- Bradycardia, hypotension and hypoventilation are rare effects.

HEENT

0.2.4.1 ACUTE EXPOSURE

- Eye exposure causes irritation and superficial injury. Chronic abuse associated with decreased visual acuity, impaired color vision, optic atrophy, and ototoxicity.

CARDIOVASCULAR

0.2.5.1 ACUTE EXPOSURE

- ACUTE INHALATION - may cause dysrhythmias (usually in chronic abusers). Bradycardia, ventricular fibrillation, and myocardial infarction have been reported.
- CHRONIC INHALATION - Chronic sniffers may develop dysrhythmias, including PVCs and supraventricular tachycardia; dilated cardiomyopathy has been reported.
- ACUTE INGESTION may cause tachycardia and hypertension.

RESPIRATORY

0.2.6.1 ACUTE EXPOSURE

- Inhalation may cause irritation, acute bronchitis, bronchospasm, pulmonary edema, pneumonitis, and asphyxia. Chronic abusers may develop respiratory failure.

NEUROLOGIC

0.2.7.1 ACUTE EXPOSURE

- ACUTE INGESTION - **Toluene** ingestion causes CNS depression.
- ACUTE INHALATION - 400 to 800 ppm: Euphoria, giddiness, tremors, nervousness, insomnia, headache, dizziness, fatigue, drowsiness, confusion, vertigo, increased reaction time; 800 ppm: ataxia, fatigue, seizures. 10,000 ppm: general anesthesia.
- CHRONIC INHALATION may cause hyperactive reflexes, peripheral neuropathy, personality changes, tremors, headaches, emotional lability, cognitive dysfunction, memory loss.

GASTROINTESTINAL

0.2.8.1 ACUTE EXPOSURE

- Ingestion or inhalation may cause vomiting, abdominal

cramps, and diarrhea.

HEPATIC

0.2.9.1 ACUTE EXPOSURE

- Rarely hepatorenal failure has been attributed to **toluene** abuse or occupational exposure. Hepatomegaly and impaired liver function has also been reported.

GENITOURINARY

0.2.10.1 ACUTE EXPOSURE

- Transient distal renal tubular acidosis (RTA), with hyperchloremic metabolic acidosis, hypokalemia, and urine pH >5.5, is common in hospitalized paint sniffers. negative.
- Proximal RTA or Fanconi's syndrome is less common (urine pH >5.5, uricosuria, hypophosphatemia, hypocalcemia).
- Isolated cases of irreversible renal insufficiency, glomerulonephritis, focal segmental glomerulosclerosis, acute interstitial nephritis, and renal failure secondary to myoglobinuria have been reported.

ACID-BASE

0.2.11.1 ACUTE EXPOSURE

- Hyperchloremic metabolic acidosis common in hospitalized **toluene** abusers.

FLUID-ELECTROLYTE

0.2.12.1 ACUTE EXPOSURE

- Hypokalemia, metabolic acidosis, and hypophosphatemia are typical; hypercalcemia and hypouricemia less frequent. Hypocalcemia and precipitation of tetany has occurred during correction of acidemia.
- Patients with weakness may have severe fluid/electrolyte imbalance.

DERMATOLOGIC

0.2.14.1 ACUTE EXPOSURE

- Prolonged contact may cause drying and defatting or superficial burns.

MUSCULOSKELETAL

0.2.15.1 ACUTE EXPOSURE

- Rhabdomyolysis is common in chronic **toluene** abusers. Severe muscle weakness is a common presentation in chronic abuse.

PSYCHIATRIC

0.2.18.1 ACUTE EXPOSURE

- Psychiatric disorders are common in chronic **toluene** abusers; including bizarre behavior, acute paranoid psychosis, confusion, visual and auditory hallucinations, mood lability, and decreased IQ.

REPRODUCTIVE HAZARDS

- Multiple physical deformities, with signs similar to fetal alcohol syndrome, microencephaly, CNS dysfunction, and variable growth deficiencies have occurred in infants born to mothers who abused **toluene** during pregnancy.

GENOTOXICITY

- There is conflicting information in the literature regarding the potential of **toluene** to cause DNA strand breaks. **Toluene** was not mutagenic in the Ames assay. Chromosome damage has been reported.

Laboratory:

- **Toluene** may be measured in the breath and blood; hippuric acid and cresol metabolites may be measured in the urine.
- Obtain a baseline CBC and monitor renal and hepatic function tests, urinalysis (including urine pH) electrolytes, and CPK. Monitor arterial blood gases in symptomatic patients.

Treatment Overview:

ORAL EXPOSURE

- EMESIS - Emesis is probably not indicated due to the possibility for aspiration of gastric contents.
- GASTRIC LAVAGE may be indicated when the patient has ingested a large quantity of **toluene**, or there is a large amount of benzene contamination, and emesis is contraindicated (obtunded, comatose, convulsing). The potential toxicity of the amount ingested must be weighed against the substantial risk of aspiration.

1. GASTRIC LAVAGE: Consider after ingestion of a potentially life-threatening amount of poison if it can be performed soon after ingestion (generally within 1 hour). Protect airway by placement in Trendelenburg and left lateral decubitus position or by endotracheal intubation. Control any seizures first.

a. CONTRAINDICATIONS: Loss of airway protective reflexes or decreased level of consciousness in unintubated patients; following ingestion of corrosives; hydrocarbons (high aspiration potential); patients at risk of hemorrhage or gastrointestinal perforation; and trivial or non-toxic ingestion.

- ACTIVATED CHARCOAL: Administer charcoal as slurry (240 mL water/30 g charcoal). Usual dose: 25 to 100 g in adults/adolescents, 25 to 50 g in children (1 to 12

years), and 1 g/kg in infants less than 1 year old.
- MONITOR FLUID and ELECTROLYTE STATUS CAREFULLY. Correct hypokalemia with intravenous potassium.
- MONITOR PATIENT for RESPIRATORY DISTRESS.
- MONITOR EKG and VITAL SIGNS REGULARLY. Use epinephrine cautiously if indicated.
- CHRONIC EXPOSURE - Evaluate renal and liver function.

INHALATION EXPOSURE
- DECONTAMINATION: Move patient to fresh air. Monitor for respiratory distress. If cough or difficulty in breathing develops, evaluate for respiratory tract irritation, bronchitis, or pneumonitis. Administer 100 percent humidified supplemental oxygen with assisted ventilation as required.
- MONITOR FLUID and ELECTROLYTE STATUS CAREFULLY. Correct hypokalemia with potassium. CAUTION - Hypocalcemia may ensue following fluid and electrolyte replenishment.
- MONITOR for RESPIRATORY DISTRESS, assure airway patency and adequacy of ventilation and oxygenation.
- MONITOR EKG and VITAL SIGNS REGULARLY. Use epinephrine cautiously if indicated.

EYE EXPOSURE
- DECONTAMINATION: Exposed eyes should be irrigated with copious amounts of tepid water for at least 15 minutes. If irritation, pain, swelling, lacrimation, or photophobia persist, the patient should be seen in a health care facility.

DERMAL EXPOSURE
- DECONTAMINATION: Wash exposed area extremely thoroughly with soap and water. A physician may need to examine the area if irritation or pain persists.

Range of Toxicity:

- Ingestion - 60 mL lethal in an adult. Inhalation - 600 to 800 ppm for 3 hrs caused fatigue, nausea, confusion, ataxia; 10,000 ppm causes general anesthesia.

[Rumack BH: POISINDEX(R) Information System. Micromedex, Inc., Englewood, CO, 2001; CCIS Volume 107, edition exp February, 2001. Hall AH & Rumack BH (Eds):TOMES(R) Information System. Micromedex, Inc., Englewood, CO, 2001; CCIS Volume 107, edition exp February, 2001.]
PEER REVIEWED

Antidote and Emergency Treatment:

Basic treatment: Establish a patent airway. Suction if necessary. Watch for signs of respiratory insufficiency and assist ventilations if necessary. Administer oxygen by nonrebreather mask at 10 to 15 L/min. Monitor for pulmonary edema and treat if necessary ... . Monitor for shock and treat if necessary ... . For eye contamination, flush eyes immediately with water. Irrigate each eye continuously with normal saline during transport ... . Do not use emetics. For ingestion, rinse mouth and administer 5 ml/kg up to 200 ml of water for dilution if the patient can swallow, has a strong gag reflex, and does not drool. Administer activated charcoal ... . /Aromatic hydrocarbons and related compounds/
[Bronstein, A.C., P.L. Currance; Emergency Care for Hazardous Materials Exposure. 2nd ed. St. Louis, MO. Mosby Lifeline. 1994.,p. 181-2]**PEER REVIEWED**

Advanced treatment: Consider orotracheal or nasotracheal intubation for airway control in the patient who is unconscious or in respiratory arrest. Positive-pressure ventilation techniques with a bag-valve-mask device may be beneficial. Monitor cardiac rhythm and treat arrhythmias if necessary ... . Start an IV with D5W /SRP: "To keep open", minimal flow rate/. Use lactated Ringer's if signs of hypovolemia are present. Watch for signs of fluid overload. Consider drug therapy for pulmonary edema ... . Treat seizures with diazepam (Valium) ... . Use proparacaine hydrochloride to assist eye irrigation ... . /Aromatics hydrocarbons and related compounds/
[Bronstein, A.C., P.L. Currance; Emergency Care for Hazardous Materials Exposure. 2nd ed. St. Louis, MO. Mosby Lifeline. 1994. 182]**PEER REVIEWED**

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Emergency Medical Treatment:

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PEER REVIEWED

TOLUENE

CASRN: 108-88-3

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[Bronstein, A.C., P.L. Currance; Emergency Care for Hazardous Materials Exposure. 2nd ed. St. Louis, MO. Mosby Lifeline. 1994.,p. 181-2]**PEER REVIEWED**

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[Bronstein, A.C., P.L. Currance; Emergency Care for Hazardous Materials Exposure. 2nd ed. St. Louis, MO. Mosby Lifeline. 1994. 182]**PEER REVIEWED**

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Animal Toxicity Studies:

Evidence for Carcinogenicity:

Evaluation: There is inadequate evidence for the carcinogenicity of **toluene** in humans. There is evidence suggesting lack of carcinogenicity of **toluene** in experimental animals. Overall evaluation: **Toluene** is not classifiable as to its carcinogenicity to humans (Group 3).
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V71 855 (1999)]**PEER REVIEWED**

CLASSIFICATION: D; not classifiable as to human carcinogenicity. BASIS FOR CLASSIFICATION: No human data and inadequate animal data. **Toluene** did not produce positive results in the majority of genotoxic assays. HUMAN CARCINOGENICITY DATA: None.
[U.S. Environmental Protection Agency's Integrated Risk Information System (IRIS) on Toluene (108-88-3) Available from: http://www.epa.gov/ngispgm3/iris on the Substance File List as of March 15, 2000]**PEER REVIEWED**

A4. A4= Not classifiable as a human carcinogen.
[American Conference of Governmental Industrial Hygienists. TLVs and BEIs. Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. Cincinnati, OH. 2000. 67]**QC REVIEWED**

Non-Human Toxicity Excerpts:

A TEMPORARY INCOORDINATION WITH MUSCULAR TREMORS HAS BEEN OBSERVED IN PUPPIES & KITTENS & IN DOGS AT TWICE THERAPEUTIC DOSE LEVEL. CALVES IN POOR CONDITION SHOWED STAGGERING GAIT AND SOME COLLAPSED BUT RECOVERY WAS COMPLETE AFTER UP TO 4 HOURS. FOUR TIMES THERAPEUTIC DOSE RATE PRODUCED NO OBSERVABLE CHANGES IN ... ORGANS.
[Clarke, M. L., D. G. Harvey and D. J. Humphreys. Veterinary Toxicology. 2nd ed. London: Bailliere Tindall, 1981. 100]**PEER REVIEWED**

... /CNS DEPRESSANT/ EFFECT OF **TOLUENE** ... IS EXERTED IN 2 PHASES--A PRELIMINARY ... /CNS DEPRESSION/ FOLLOWED BY STAGE OF EXCITEMENT, MANIFESTED BY TREMOR, MUSCULAR CRAMPS AND DISTURBANCES IN BEHAVIOR ...
[Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965. 70]**PEER REVIEWED**

... SWELLING OF GLOMERULI, CYLINDERS & ALBUMIN IN URINE IN 2 ... DOGS. BUT ...

/INVESTIGATORS/ NOTE THAT THE DOGS WERE OF BREED WHICH FREQUENTLY DEVELOP INTERSTITIAL NEPHRITIS. ... HEMORRHAGIC & DEGENERATIVE LESIONS IN GOATS.
[Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965. 72]**PEER REVIEWED**

IN DOGS ... CONGESTION & HEMORRHAGIC FOCI WERE PRESENT IN LIVER; THESE LESIONS ... ALSO PRESENT IN GOATS ... CONGESTION & SOME ALVEOLAR INFLAMMATION /OF LUNG ALSO/ ... IN DOGS & ... GOATS. SPLEEN ... SHOWED SOME DIMINUTION OF LYMPHOID FOLLICLES & PLAQUES OF HEMOSIDEROSIS.
[Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965. 71]**PEER REVIEWED**

EFFECTS IN CATS EXPOSED TO 7800 PPM (31.0 MG/L)/6 HR: CNS EFFECTS, MYDRIASIS, MILD TREMORS, PROSTRATION IN 80 MIN, LIGHT ANESTHESIA IN 2 HR. /FROM TABLE/
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1327]**PEER REVIEWED**

INTRATRACHEAL ADMIN /TO CATS/ WITH CHRONICALLY IMPLANTED ELECTRODES INDUCED SEIZURES ALONG WITH BEHAVIORAL DISTURBANCES SUCH AS NODDING, TWITCHING & APPARENT HALLUCINATIONS.
[CONTRERAS CM ET AL; ELECTROENCEPHALOGR CLIN NEUROPHYSIOL 46 (3): 290 (1979)]**PEER REVIEWED**

... RATS /EXPOSED/ TO 1500 MG/CU M OF AIR FROM DAY 1 THROUGH 8 OR 1000 MG/CU M FOR 8 HR DAILY FROM DAY 1 THROUGH DAY 21 /OF GESTATION/ ... /WITH/ NO TERATOGENIC EFFECT. SOME FETAL GROWTH RETARDATION ... @ HIGHER DOSE ... MICE WERE EXPOSED DURING DAYS 6-13 TO 1500 MG/CU M OF AIR WITH SIMILAR RESULTS.
[Shepard, T.H. Catalog of Teratogenic Agents. 5th ed. Baltimore, MD: The Johns Hopkins University Press, 1986. 1438]**PEER REVIEWED**

/GAVAGING/ MICE /WITH/ 1.0 MG/KG ON DAYS 6 THROUGH 15 /OF GESTATION/ ... INCR CLEFT PALATE IN THE OFF-SPRING.
[Shepard, T.H. Catalog of Teratogenic Agents. 5th ed. Baltimore, MD: The Johns Hopkins University Press, 1986. 1438]**PEER REVIEWED**

TOLUENE WAS UNABLE TO REVERT SALMONELLA TYPHIMURIUM STRAINS TA1535, TA1537, TA1538, TA98 AND TA100 IN THE AMES SALMONELLA/MICROSOME ASSAY, EITHER WITH OR WITHOUT METABOLIC ACTIVATION BY S9 MIX FROM LIVERS OF RATS EITHER UNTREATED OR INDUCED WITH AROCLOR 1254.
[BOS RP ET AL; MUTAT RES 88: 273 (1981)]**PEER REVIEWED**

FOLLOWING IP ADMIN OF 1 ML **TOLUENE**/KG DAILY FOR 21 DAYS TO RATS, MIXED-FUNCTION OXYGENASE ACTIVITY INCREASED 33.8% IN LIVER BUT WAS UNCHANGED IN BRAIN.
[CHAND P, CLAUSEN J; BULL ENVIRON CONTAM TOXICOL 28 (5): 542

(1982)]**PEER REVIEWED**

TOLUENE & M-XYLENE CAUSED MUSCULAR WEAKNESS & EQUILIBRIUM DISTURBANCES IN THE RAT FOLLOWING IP ADMIN. THE LOCOMOTOR (OPEN-FIELD BEHAVIOR) & RUNNING ACTIVITY (WHEEL-RUNNING) IN THE RAT WAS MOST AFFECTED BY **TOLUENE**. THESE DIFFERENCES WERE RELATED TO THE DIFFERENCES IN THE STIMULATORY EFFECTS OF THE SOLVENTS ON THE CNS.
[PAKSY KA ET AL; ACTA PHYSIOL ACAD SCI HUNG 59 (4): 317 (1982)]**PEER REVIEWED**

RATS WERE EXPOSED TO **TOLUENE** OR N-HEXANE OR A MIXT OF THE 2 CMPD AT 1000-8000 PPM FOR 8 HR. ACETYLCHOLINE WAS INCR AT LOW CONCN OF THE SOLVENTS, BUT WAS GREATLY DECR AT HIGH CONCN. CHOLINE ACETYLTRANSFERASE WAS DECR SIGNIFICANTLY AT HIGH CONCN OF THE MIXT. ACETYLCHOLINE ESTERASE ACTIVITY WAS INCR BY THE SOLVENTS.
[HONMA T; TOXICOL LETT 16 (1-2): 17 (1983)]**PEER REVIEWED**

In skin painting studies with CF1, CH, and BaH strains of mice, 0.05 to 0.1 ml/mouse was applied to 25 mice/sex/strain for 52 weeks. Results were negative for tumor development.
[USEPA; Ambient Water Quality Criteria Doc: Toluene p.C-26 (1980) EPA 440/5-80-075]**PEER REVIEWED**

Intraperitoneal admin of 250, 500, or 1,000 mg/kg at 0 and 24 hr failed to give positive results in micronucleus test with Swiss mice.
[USEPA; Ambient Water Quality Criteria Doc: Toluene p.14-6 (1980) EPA 440/5-80-075]**PEER REVIEWED**

... Groups of rats were trained on the conditioned avoidance response task during the last week of a 5 week exposure to 1400 or 1200 ppm **toluene** (14 hr/day, 7 days/week) or during the first or third weeks after the exposure ended. None of the three groups ... were able to acquire the auditory condition avoidance response ... . Subsequent tests ... revealed that hearing with these rats was unimpaired at 4 KHz, slightly impaired at 8 KHz, and markedly impaired at 12 KHz and above.
[Pryor GT et al; Neurobehav Toxicol Terat 5 (1): 53-7 (1983)]**PEER REVIEWED**

Pregnant CD-1 mice were housed singly in multicompartment cages in inhalation chambers and exposed to **toluene** at a concentration of 0, 750, or 1500 mg/cu m (0, 200, or 400 ppm) for 7 hrs/day from day 7 through day 16 of gestation. The mice were killed on day 17 of gestation and the fetuses were removed and examined. Maternal weight gain was not affected by **toluene** exposure but the liver to body weight ratio was significantly reduced. The treated dams showed no significant differences in the average number of implantation sites, number of live fetuses, fetal mortality, or fetal body weight at either **toluene** concentration compared to control values. The incidence of enlarged renal pelvis was significantly greater in fetuses exposed to 200 ppm than in the fetuses exposed to 400 ppm or in the controls. A shift in rib profile (number of fetuses with 13 ribs) was observed in the higher **toluene** concentration group, and this shift was significantly different from the rib profile of controls. There was an increase in the total activity of lactic dehydrogenase activity in the brain of the dams from the 400 ppm group. The total activity of lactic dehydrogenase in the **toluene** exposed pups did not differ significantly from the controls for liver, heart, lung, or kidney, but the brain lactic dehydrogenase activity

of the treated group was slightly greater than the control value.
[Courtney KD et al; Fundam Appl Toxicol 6: 145-54 (1986)]**PEER REVIEWED**

Behavioral toxicity of **toluene** was assessed in mice confined in a 20 liter hermetically sealed chamber for several hours. **Toluene** was introduced through a port and volatilized by a hot plate. Samples of chamber air for analysis were taken through another port. A smaller mesh cage held the mouse within the larger chamber. Schedule-controlled responding was developed by arranging that a response, breaking a beam of light, was followed by mild (under an F1 60 sec) schedule. Responding was much more rapid in the presence of stimuli correlated with the F1 schedule than when the schedule was not operating. Standard sessions consisted of alternating series of 8 consecutive F1 60 sec and inter-series 30 min time-outs. Concentration-effect curves were determined by exposing a mouse to incremental additions of **toluene** at 30 min intervals. **Toluene** increased the rate of responding in most mice at levels of about 700 ppm. Higher concentrations progressively reduced responding. The ED50 (the concentration reducing responding by 50%) averaged 1657 ppm in 10 mice. It is estimated that there is a 1/1000 chance /ED001/ of the responding of a mouse being reduced by as much as 10% by a concentration of **toluene** of 69 ppm.
[Glowa JR et al; J Environ Pathol Toxicol Oncol 6 (5-6): 153-68 (1986)]**PEER REVIEWED**

Sixteen rats were chronically implanted with bipolar electrodes in the hipocampal regions containing cells generating electric theta-activity. The animals were divided into 4 groups of which 2 were exposed to 500 ppm of **toluene** in inhalation chambers, for 8 or 16 hours per day for 5 days per week in 12 weeks respectively, and 2 served as controls. The hippocampal electric activity was recorded 48 hours after each weekly exposure. Frequencies of theta-activity in the exposed groups were found to differ from their respective control group by variance analysis. Each point on the frequency versus time plot were further analysed by Student's t-test. Compared to the non-exposed group the eight hours daily exposed showed an initial period of increased frequency of the regular theta-waves together with an increased incidence of theta-activity after 1-2 weeks of exposure. In the sixteen hours daily exposed rats two weeks of **toluene** inhalation produced a significant reduction in the theta-wave frequency. This change was also reached after either weeks of exposure in the eight hours daily exposed group. At this moment the theta-activity was frequency disrupted by short amplitude irregular waves, a phenomen which increased gradually throughout the rest of the exposure period. The average blood concentration of **toluene** was 16.7 ug/ml and 17.7 ug/ml and not significantly different for the eight and sixteen hours exposed groups respectively.
[Naalsund LU; Acta Pharmacol Toxicol 59 (4): 325-31 (1988)]**PEER REVIEWED**

The effects of **toluene** vapors on brain lipid changes were investigated in male Sprague-Dawley rats. The animals (8/group) were continuously exposed to 320 ppm **toluene** for 30 days. Controls were exposed to air. Exposed animals showed decreased body weight ($p< 0.01$), decreased brain weight ($p< 0.01$), and a decrease in the weight of the cerebral cortex ($p< 0.05$) when compared to controls. In the cerebral cortex of exposed rats, total phospholipids was reduced ($p< 0.001$), there was an increase in phosphatidic acid ($p< 0.05$) and a decrease in a minor fatty acid of ethanolamine phosphoglyceride ($p< 0.05$). No changes in lipids were found in the brain stem.
[Kyrklund T et al; Toxicology 45: 123-33 (1987)]**PEER REVIEWED**

With the intention of investigating possible morphological alterations effected by **toluene** in the

developing CNS, rat pups were exposed to 100 ppm and 500 ppm of atmospheric **toluene** from postnatal day 1 until sacrifice at postnatal day 28, when the hippocampal region (area dentata, Ammon's horn, subiculum) was examined by light microscope and alterations in the volumes of the layers of the subdivisions were determined. The layers of Ammon's horn and the subiculum were not affected qualitatively or quantitatively by the 500 ppm exposure. Within the area dentata, the volume of the granule cell layer was 6% smaller in animals exposed to 100 ppm and 13% smaller in animals exposed to 500 ppm than they were in controls. The volumes of the hilus, which is a terminal field of granule cell axons, and the commissural-association zone of the dentate molecular layer, which is the terminal field of the hilar projection to the granule cells, were smaller (12% and 19%) in animals exposed to 500 ppm than they were in controls. Argyrophilic cells were found in the granule cell layer of all animals exposed to 500 ppm. Pronounced granule cell degeneration was found in one animal exposed to 500 ppm. The granule cell layer of animals exposed to 100 ppm appeared qualitatively normal. The alterations reported here support the few earlier reports of morphological alterations in the CNS of adult laboratory animals. Effects of **toluene** similar to those described, that is alterations in specific neuron populations and their afferent and efferent terminal fields may complement changes in neurophysiology and behavior that have been observed in prenatally and perinatally exposed rodent pups. Causal relationships, however, remain to be elucidated.
[Slomianka L et al; Toxicol 62 (2): 189-202 (1990)]**PEER REVIEWED**

The aim of the present study was to investigate the effects of **toluene** on fetal development in well nourished and malnourished rats. Long-term behavioral consequences after in utero exposure were also studied. **Toluene** (1.2 g/kg sc) was administered daily to well nourished and to malnourished (food restricted to 50% of ad libitum intake) pregnant rats, during the second (8-15 days) or the third week of pregnancy (14-20 days). Offspring were evaluated for malformation, development of the skeleton, prenatal growth of the brain and liver, postnatal growth and long lasting behavioral effects. In utero exposure to **toluene** during the third week of pregnancy resulted in low body weight at birth, which persisted in the male offspring into adulthood. Malnutrition increased fetal susceptibility to the effects of **toluene** as indicated by evaluation of the development of the skeleton. Behavioral tests performed when the pups were 30 and 90 days old showed effects of in utero malnutrition (increased ambulation and worse performance in a shuttle box), but no behavioral effects related to **toluene** exposure were detected. These data indicate that in utero exposure to **toluene** can have long lasting effects on body growth and that maternal malnutrition increases the risk for **toluene** fetotoxicity.
[Silva V AD et al; Toxicol 64 (2): 155-68 (1990)]**PEER REVIEWED**

Toluene did not induce gene mutations in Salmonella typhimiurium strain TA98, TA100, TA1535, or TA1537 with or without exogenous metabolic activation. In the mouse lymphoma assay, **toluene** gave an equivocal response with and without exogenous metabolic activation. **Toluene** did not induce sister chromatid exchanges or chromosomal aberrations in Chinese hamster ovary cells in the presence or absence of exogenous metabolic activation.
[DHHS/NTP; Toxicology and Carcinogenesis Studies of Chlorobenzene in F344/N Rats and B6C3F1 Mice (Inihalation Studies) p.4 (1990) Technical Rpt Series No. 371 NIH Pub No. 90-2826]**PEER REVIEWED**

... **Toluene** can alter learned behavior at concentrations below anesthetic levels but, in general, above 1000 ppm.
[Klaassen, C.D., M.O. Amdur, Doull J. (eds.). Casarett and Doull's Toxicology. The Basic Science of Poisons. 5th ed. New York, NY:

McGraw-Hill, 1995. 747]**PEER REVIEWED**

Toluene was injected into the yolk sac of fresh fertile chicken eggs prior to incubation. Hatchability of the eggs was 85%, 25%, and 0 with exposures of 4.3, 8.7, and 17.4 mg/egg, respectively.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47 96 (1989)]**PEER REVIEWED**

Toluene was reported to induce chromosomal aberrations in the bone marrow cells of male albino rats after chronic inhalation exposure to 5.4 or 50.7 mg/cu m on 4 hr/day, five days/wk for four months or after sc injection of 0.8 g/kg bw. Chromosomal aberrations in bone marrow cells were reported following sc injection of 1 g/kg bw daily for 12 days to male albino rats.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47 98 (1989)]**PEER REVIEWED**

Toluene and benzene administered concurrently were reported to have an additive effect on induction of chromosomal aberrations. **Toluene** reduced the number of sister chromatid exchanges induced by benzene when both compounds were administered intraperitoneally to DBA/2 mice and reduced the clastogenic activity of benzene when the two compounds were simultaneously administered orally to CD-1 mice, intraperitoneally to Sprague-Dawley rats, or subcutaneously to NMRI mice.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47 99 (1989)]**PEER REVIEWED**

Animal studies in mice exposed to **toluene** at concentrations of 2.5-500 ppm demonstrated decreased host defense to respiratory infections.
[Sullivan, J.B. Jr., G.R. Krieger (eds.). Hazardous Materials Toxicology-Clinical Principles of Environmental Health. Baltimore, MD: Williams and Wilkins, 1992. 1092]**PEER REVIEWED**

The cardiovascular response of 25 mongrel dogs following exposure to 30,000 ppm **toluene** for 9-10 min was complex. For most of the animals, there was no change in electrocardiogram readings for the first 3-4 min of exposure. The heartbeat then became rapid for several minutes, and was followed by a period of bradycardia. Immediately before death ventricular fibrillation was noted. ... Four of the dogs were particularly sensitive, their ventricular arrhythmias were transient and accompanied by fluctuations of blood pressure. The authors suggested that **toluene** had a direct effect on the septal and ventricular muscles of the heart which permitted the development of fatal arrhythmias in sensitive dogs.
[Ikeda N et al; Forensic Sci Intern 44: 151-8 (1990) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.31 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

Mice exposed for 3 hr to **toluene** at concentrations of 2.5-500 ppm exhibited increased, but not dose-related, susceptibility to respiratory infections when challenged by Streptococcus zooepidemicus.

Pulmonary bactericidal activity was decreased at concentrations of 2.5 ppm and 100-500 ppm but not at concentrations of 5-50 ppm. There was no effect on susceptibility to infection with a **toluene** exposure of 1 ppm for 3 hr, 5 days (3 hr/day) or 4 wk (3 hr/day). The bactericidal activity of the lung was decreased during the 5-day treatment but not with the 4-wk treatment. The authors hypothesized that **toluene** exerted an adverse effect on alveolar macrophage function, thereby decreasing disease resistance.
[Aranyi C et al; Toxicol Lett 25: 103-10 (1985) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.39 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

Studies have demonstrated that **toluene** can produce subtle changes in the auditory system. Intermediate exposure to **toluene** produced a permanent loss of hearing in the high frequency range (approximately 16 kHz) in rats exposed to 1200 ppm for 5-9 wk or 1000 ppm for 2 wk.
[Pryor GT, Rebert CS; Neurotoxicology 13: 225-34 (1992) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.44 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

In 3-day-old rats, daily 15 min exposures to **toluene** resulted in a dose-related increase in righting-reflex latency time. At each dose the righting-reflex latency decreased over the first 4 wk of exposure indicating that the animals had developed at least partial tolerance to the **toluene**. During the second 4-wk period, latencies increased again at the higher doses but were never as great as they were for the initial **toluene** exposure. The results for the second 4-wk period showed that there were limitations to the adaptive response at the higher **toluene** doses and that there were cumulative effects of exposure at these doses. Tolerance was probably the result of induction of **toluene** metabolizing enzymes.
[Lorenzana-Jimenez M, Salas M; Neurotoxicol Teratol 12: 353-7 (1990) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.45 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

Concentrations of 480 ppm and above decreased the ability of trained rats to perform a sequence of lever press actions associated with a reward (milk). During training, the rats were divided into two groups. The reward presentation for one group was not accompanied by any noticeable external events. For the second group, the reward presentation was accompanied by light and sound stimuli. The effects of **toluene** on performance were less severe with the rats trained using the light and sound reinforcement. This suggests that behavior associated with external signals is less subject to disruption by **toluene** than behavior that is not accompanied by external reinforcement.
[Wood RW et al; Toxicol Appl Pharmacol 68: 462-72 (1983) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.45 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

Age ... influences neurological response after exposure to **toluene**. Young rats (50 days old) were affected by **toluene** to a lesser extent than older rats (120 days old) based on several measurements of escape latency 30 days after exposure to 30,000-40,000 ppm for 15 min/day.
[Castilla-Serna L et al; Arch Invest Med 22: 295-301 (1991) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances &

Disease Registry; Toxicological Profile for Toluene (Update) p.46 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

Toluene exposure ... changes sleep patterns in animals. Both single episodes of **toluene** exposure (about 1000 ppm) and subchronic 8 hr/day exposures for 3 wk (about 600 ppm), changed patterns of sleep and wakefulness in rats. After the single exposures, there was a decrease in wakefulness and an increase in slow-wave sleep; a prolonged sleep latency was apparent for the 2 days following exposure. Latency was defined as the time interval between the end of the exposure period and the beginning of a particular phase of the sleep cycle. Following the 3 wk exposures, there was an increase in wakefulness during the dark period on the 2 days after exposure and a decrease in slow wave sleep on the first day.
[Arito H et al; Arch Toxicol 62: 76-80 (1988) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.46 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

Brain levels of norepinephrine, dopamine, serotonin, vanillylmandelic acid, homovanillic acid, and 5-hydroxyindolacetic acid were altered in six areas of the brain in male CD-1 mice administered **toluene** (5-105 mg/kg/day) in their drinking water for a 28-day period. Significant increases of norepinephrine, dopamine, and serotonin were present in the hypothalamus at all dose levels. The maximum increase occurred with the 22 mg/kg/day dose and there were lesser increases for both the 5 and 105 mg/kg/day doses, giving biphasic response. Roughly similar fluctuations were seen in the concentrations of vanillylmandelic acid and homovanillic acid, which are metabolites of dopamine and norepinephrine and 5-hydroxyindolacetic acid, a serotonin metabolite. In corpus striatum, the levels of dopamine and serotonin were significantly increased at the two highest doses. The level of vanillylmandelic acid was also increased significantly at the same doses. In the medulla oblongata, the concentrations of norepinephrine, vanillylmandelic acid, and 5-hydroxyindolacetic acid were significantly increased at the 22 mg/kg/day dose, but not at the other doses, while the levels of serotonin were significantly increased at the 22 and 105 mg/kg/day doses. Norepinephrine concentrations were elevated in the midbrain. ...
[U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.61 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

To identify the frequency range most sensitive to **toluene**-induced auditory damage, the auditory function of adult Long-Evans rats exposed to 1750 ppm of **toluene** (6 h/day, 5 days/week, 4 weeks), was tested by recording auditory-evoked potentials directly from the round window of the cochlea. The present electrocochleographic findings do not support a specific mid- to high-frequency loss of auditory sensitivity. On the contrary, the electrophysiologic data, obtained for audiometric frequencies ranging from 2 to 32 kHz, showed a hearing deficit not only in the mid-frequency region (12-16 kHz), but also in the mid-low-frequency region (3-4 kHz). Actually, the effect of **toluene** was independent of the frequency in our experimental conditions. Histological analysis was consistent with electrophysiologic data because a broad loss of outer hair cells occurred in both mid- and mid-apical coil of the organ of Corti.
[Lataye R et al; Neurotoxicol Teratol 21 (3): 267-76 (1999)]**PEER REVIEWED**

National Toxicology Program Studies:

Long-term studies were conducted by exposing groups of 60 rats /F344/N/ of each sex to 0, 600, or 1,200 ppm **toluene** by inhalation, 6.5 hours per day, 5 days per week. Groups of 60 /B6C3F1/ mice of each sex were exposed at 0, 120, 600, or 1,200 ppm on the same schedule. ... Animals were exposed to **toluene** for 103 weeks. Nephropathy was seen in almost all rats, and the severity was somewhat increased in exposed rats. A rare renal tubular cell carcinoma in a female rat and an equally uncommon sarcoma of the kidney in another female rat were seen in the 1,200 ppm exposure group. Erosion of the olfactory epithelium and degeneration of the respiratory epithelium were increased in exposed rats. Inflammation of the nasal mucosa and metaplasia of the olfactory epithelium were increased in exposed female rats. A rare squamous cell carcinoma of the nasal mucosa was seen in one female rat at 1,200 ppm. A squamous cell papilloma of the forestomach was observed in one female rat at 1,200 ppm, and a squamous cell carcinoma was observed in a second female rat at 1,200 ppm. No chemically related neoplasms were found in male rats, and the one nasal, two kidney, and two forestomach neoplasms observed in female rats were considered not to be associated with inhalation exposure to **toluene**. For mice, no biological important increases were observed for any nonneoplastic or neoplastic lesions.
[DHHS/NTP; Toxicology and Carcinogenesis Studies of Chlorobenzene in F344/N Rats and B6C3F1 Mice (Inhalation Studies) p.4 (1990) Technical Rpt Series No. 371 NIH Pub No. 90-2826]**PEER REVIEWED**

Non-Human Toxicity Values:

LD50 Rat oral 2.6 to 7.5 g/kg
[DHHS/NTP; Toxicology and Carcinogenesis Studies of Chlorobenzene in F344/N Rats and B6C3F1 Mice (Gavage Studies) p.16 (1990) Technical Rpt Series No. 371 NIH Pub No. 90-2826]**PEER REVIEWED**

LD50 Rabbit dermal 14.1 ml/kg
[DHHS/NTP; Toxicology and Carcinogenesis Studies of Chlorobenzene in F344/N Rats and B6C3F1 Mice (Gavage Studies) p.16 (1990) Technical Rpt Series No. 371 NIH Pub No. 90-2826]**PEER REVIEWED**

LD50 Rat (female) ip 1.64 g/kg
[DHHS/NTP; Toxicology and Carcinogenesis Studies of Chlorobenzene in F344/N Rats and B6C3F1Mice (Inhalation Studies) p.16 (1990) Technical Rpt Series No. 371 NIH Pub No. 90-2826]**PEER REVIEWED**

LD50 MOUSE IP 1.15 G/KG
[KOGA K, OHMIYA Y; J TOXICOL SCI 3 (1): 25 (1978)]**PEER REVIEWED**

LD50 Rat oral 5000 mg/kg
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 3190]**PEER REVIEWED**

LD50 Rat ip 1332 mg/kg
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 3190]**PEER REVIEWED**

LD50 Rat iv 1960 mg/kg

[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 3190]**PEER REVIEWED**

LC50 Mouse ihl 400 ppm/24 hr
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 3190]**PEER REVIEWED**

LD50 Mouse ip 59 mg/kg
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 3190]**PEER REVIEWED**

LD50 Mouse sc 2250 mg/kg
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 3190]**PEER REVIEWED**

LD50 Mouse ip 640 mg/kg
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 3190]**PEER REVIEWED**

LD50 Rabbit skin 12,124 mg/kg
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 3190]**PEER REVIEWED**

... The LC50 for **toluene** in mice is 5320 ppm/8 hr /via inhalation/ ...
[Klaassen, C.D., M.O. Amdur, Doull J. (eds.). Casarett and Doull's Toxicology. The Basic Science of Poisons. 5th ed. New York, NY: McGraw-Hill, 1995. 746]**PEER REVIEWED**

As the duration of **toluene** inhalation exposure increased, the LC50 in rats decreased from 26,700 ppm for 1 hr, to 12,200 ppm for 2-2.5 hr, to 8000 ppm for 4 hr.
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Volumes I,II, III. Cincinnati, OH: ACGIH, 1991. 1568]**PEER REVIEWED**

Ecotoxicity Values:

LC50 FOR BLUEGILL WAS 17 MG/L/24 HR & 13 MG/L/96 HR (95% CONFIDENCE LIMIT 11-15 MG/L) @ 21-23 DEG C AFTER EXPOSURE TO **TOLUENE**. /CONDITIONS OF BIOASSAY NOT SPECIFIED/
[BUCCAFUSCO RJ ET AL; BULL ENVIRONM CONTAM TOXICOL 26 (4): 446-52 (1981)]**PEER REVIEWED**

LC50 Palaemonetes pugio (grass shrimp) 9.5 mg/l/96 hr /Conditions of bioassay not specified/
[Verschueren, K. Handbook of Environmental Data on Organic Chemicals. 3rd ed. New York, NY: Van Nostrand Reinhold Co., 1996. 1727]**PEER REVIEWED**

LC50 Cancer magister (crab larvae stage I) 28 mg/l/96 hr /Conditions of bioassay not specified/
[Verschueren, K. Handbook of Environmental Data on Organic Chemicals. 3rd ed. New York, NY: Van Nostrand Reinhold Co., 1996. 1727]**PEER REVIEWED**

LC50 Crangon franciscorum (shrimp) 4.3 mg/l/96 hr /Conditions of bioassay not specified/
[Verschueren, K. Handbook of Environmental Data on Organic Chemicals. 3rd ed. New York, NY: Van Nostrand Reinhold Co., 1996. 1728]**PEER REVIEWED**

LC50 Pimephales promelas (fathead minnow) 56-34 mg/l/24-96 hr /Conditions of bioassay not specified/
[Verschueren, K. Handbook of Environmental Data on Organic Chemicals. 3rd ed. New York, NY: Van Nostrand Reinhold Co., 1996. 1728]**PEER REVIEWED**

LC50 Lebistes reticulatus (guppy) 63-59 mg/l/24-96 hr /Conditions of bioassay not specified/
[Verschueren, K. Handbook of Environmental Data on Organic Chemicals. 3rd ed. New York, NY: Van Nostrand Reinhold Co., 1996. 1729]**PEER REVIEWED**

LC50 Channel catfish 240 mg/l 96 hr /Conditions of bioassay not specified/
[Environment Canada; Tech Info for Problem Spills: Toluene p.71-75 (1981)]**PEER REVIEWED**

LC50 Pimephales promelas (fathead minnow) 34.27 mg/l 96 hr (95% Confidence Limits= 22.83-45.86 mg/l) /Conditions of bioassay not specified/
[Pickering QH, Henderson C; J Water Pollution Control Fed 38: 1419-1429 (1966) as cited in NRC; Alkyl Benzenes p.352 (1981)]**PEER REVIEWED**

LC50 Carassius auratus (goldfish) 57.68 mg/l 96 hr (95% Confidence Limits= 48.87-68.75 mg/l) /Conditions of bioassay not specified/
[Pickering QH, Henderson C; J Water Pollution Control Fed 38: 1419-1429 (1966) as cited in NRC; Alkyl Benzenes p.352 (1981)]**PEER REVIEWED**

LC50 Lebistes reticulatus (guppy) 59.30 mg/l 96 hr (95% Confidence Limits= 50.87-70.34 mg/l) /Conditions of bioassay not specified/
[Pickering QH, Henderson C; J Water Pollution Control Fed 38: 1419-1429 (1966) as cited in NRC; Alkyl Benzenes p.352 (1981)]**PEER REVIEWED**

LC50 Daphnia magna, (water flea) 313 mg/l 48 hr /Conditions of bioassay not specified/
[USEPA. In Depth Studies on Health and Environ Impact of Sel Water

Poll (1978) EPA 68-01-4646 as cited in NRC; Alkyl Benzenes p.356 (1981)]**PEER REVIEWED**

LC50 Nitocra spinipes (copepod) 24.2-74.2 mg/l 24 hr /Conditions of bioassay not specified/
[Potera GT; Effects of Benzene, Toluene, and Ethylbenzene on Several Important Members of the Estuarine Ecosystem Ph.D. Dissertation p.1-117 (1975) as cited in NRC; Alkyl Benzenes p.355 (1981)]**PEER REVIEWED**

LC50 Artemia salina (brine shrimp) 33 mg/l 24 hr /Conditions of bioassay not specified/
[Price KS et al; J Water Pollut Control Fed 46: 63-77 (1974) as cited in NRC; Alkyl Benzenes p.355 (1981)]**PEER REVIEWED**

LC50 Morone saxatilis (striped bass) 7.3 mg/l 96 hr /Conditions of bioassay not specified/
[Benville PE, Korn S; Calif Fish Game 63: 204-209 (1977) as cited in NRC; Alkyl Benzenes p.353 (1981)]**PEER REVIEWED**

LC50 Cyprinodon variegatus (sheepshead minnow) 277-485 mg/l 96 hr /Conditions of bioassay not specified/
[NRC; Alkyl Benzenes p.354 (1981)]**PEER REVIEWED**

LC50 Aedes aegypti-4th instar (mosquito larvae) 22 mg/l /Conditions of bioassay not specified/
[USEPA. In Depth Studies on Health Environ Impact of Sel Water Pollutants (1978) EPA 68-01-4646 as cited in NRC; Alkyl Benzenes p.362 (1981)]**PEER REVIEWED**

LC50 Calandra granaria (grain weevil) 210 mg/l /in air/
[Ferguson J, Pirie H; Ann Appl Biol 35:532-550 (1948) as cited in NRC; Alkyl Benzenes p 362 (1981)]**PEER REVIEWED**

LC50 Pimephales promelas (fathead minnows) 55-72 mg/l (embryos), 25-36 mg/l (1-day posthatch protolarvae), and 26-31 mg/l (30-day-old minnows)/ 96 hour /Conditions of bioassay not specified/
[Devlin EW et al; Bull Environ Contam Toxicol 29 (1): 12-17 (1982)]**PEER REVIEWED**

EC50 Pimephales promelas (fathead minnow) 14.6 mg/l/96 hr (confidence limit 14.0 to 15.1 mg/l), flow-through bioassay with measured concentrations, 24.7 deg C, dissolved oxygen 6.9 mg/l, hardness 45.4 mg/l calcium carbonate, alkalinity 43.4 mg/l calcium carbonate, and pH 7.89. Effect: loss of equilibrium.
[Geiger D.L., Poirier S.H., Brooke L.T., Call D.J., eds. Acute Toxicities of Organic Chemicals to Fathead Minnows (Pimephales Promelas). Vol. III. Superior,Wisconsin: University of Wisconsin-Superior, 1986. 163]**PEER REVIEWED**

LC50 Pimephales promelas (fathead minnow) 36.2 mg/l/96 hr (confidence limit 29.4 to 44.6 mg/l), flow-through bioassay with measured concentrations, 24.7 deg C, dissolved oxygen 6.9 mg/l, hardness 45.4 mg/l calcium carbonate, alkalinity 43.4 mg/l calcium carbonate, and pH 7.89.
[Geiger D.L., Poirier S.H., Brooke L.T., Call D.J., eds. Acute Toxicities of Organic Chemicals to Fathead Minnows (Pimephales

Promelas). Vol. III. Superior,Wisconsin: University of Wisconsin-Superior, 1986. 163]**PEER REVIEWED**

TSCA Test Submissions:

Neurotoxicity was determined in groups of rats (4 male and 4 female, strain not reported) exposed by inhalation to 0,100, or 1500 ppm **toluene** (purity not reported) 6 hrs/day, 5 days/week for periods up to 27 weeks. Histological sections of selected areas of the brainstem were made for the upper medulla oblongata (including dorsal and ventral cochlear and vestibular nuclei), lower metencephalon (including superior olivary nuclei, trapezoid body and ventral cochlear nuclei), upper metencephalon (including the lateral lemniscus, superior olivary nuclei, cochlear and vestibular nuclei, and inferior colliculus) and the mesencephalon-diencephalon junction (including the medial geniculate). The investigators reported that the "vast majority" of sections from animals exposed to **toluene** were indistinguishable from controls. Shrunken and darkly stained neurons were observed in the corpus trapezoid of one animal exposed to 100 ppm and another exposed to 1500 ppm **toluene**; these were present in only one section and not in sufficient quantity to be considered a positive response by the investigators. Statistical analysis of the results was not reported.
[American Petroleum Inst.; Effects of Toluene Exposure on Auditory Pathways, Final Report. (1979), EPA Document No. 40-8450019, Fiche No. OTS0507495] **UNREVIEWED**

Chronic toxicity was evaluated in male and female Sprague Dawley rats (15/sex/group) exposed to **toluene** via inhalation at 0, 100 and 1500 ppm for 6 hrs/day, 5 days/week for 26 weeks. There were significant increases in the hematocrit and hemoglobin levels in females at 1500 ppm in the 13th week. There were significant differences in females at week 26 in the following: decreased mean blood clotting time and increased mean serum glutamic pyruvic transaminase at 100 ppm level, and decreases in glucose levels at 1500 ppm. There were no significant differences between treated and control animals in urinalysis.
[American Petroleum Institute; 26 Week Inhalation Toxicity Study in the Rat (1980), EPA Document No. FYI-AX-1081-0136, Fiche No. 0136-0] **UNREVIEWED**

Teratogenicity was evaluated in mated female CRL:COBS CD (SD) BR rats (27/group) exposed to **toluene** by inhalation at nominal concentrations of 0, 100 or 400 ppm on gestation days (GD) 6-15 for 6 hrs/day. The adult female rats were sacrificed on GD 20 and examined. There were no significant differences observed between treated and control animals in the following: maternal mortality, body weights, food consumption, examination of tissues and organs at necropsy (except an insignificant number of observations of mottled lungs in 4 high-dose group rats), pregnancy rate, live litters, implantation sites, resorptions, litters with resorptions, dead pups, litters with dead pups, live pups/implantation site, mean live litter size, average pup weights, fetal sex ratio, examination of soft tissues of the head, thoracic and visceral organs, and skeletal abnormalities.
[Litton Bionetics, Inc.; Teratology Study in Rats, Toluene, Final Report (1978), EPA Document No. 87-8210353, Fiche No. OTS0205936] **UNREVIEWED**

The ability of **toluene** to induce specific locus mutations at the TK locus in cultured L5178Y mouse lymphoma cells (Mouse Lymphoma Mutagenesis Assay) was evaluated in the presence and absence of

mouse liver S9 metabolic activation. Based on preliminary toxicity tests, both nonactivated and S9-activated cultures were treated with 0.30, 0.20, 0.15, 0.10, or 0.050 ul/ml produced a range of 7 - 78% total growth for nonactivated cultures and from 60 - 138% total growth for S9-activated cultures. None of the nonactivated or activated cultures produced mutant frequencies significantly greater than the solvent (DMSO) controls.
[Litton Bionetics, Inc.; Mutagenicity Evaluation of Toluene. (1978), EPA Document No. 878210352, Fiche No. OTS0205936] **UNREVIEWED**

The mutagenicity of **toluene** was evaluated in Salmonella tester strains TA98, TA100, TA1535, TA1537 and TA1538, and the yeast Saccharomyces cerevisiae tester strain D4, both in the presence and absence of added metabolic activation by Aroclor-induced rat liver S9 fraction. Based on preliminary bacterial toxicity determinations, **toluene**, diluted with acetone, was tested for mutagenicity at concentrations up to 5.0 ul/plate using both the plate and suspension assay methods. **Toluene** did not cause a positive response in any of the bacterial or yeast tester strains, either with or without metabolic activation.
[Litton Bionetics, Inc.; Mutagenicity Evaluation of Toluene. (1978), EPA Document No. 878210352, Fiche No. OTS0205936] **UNREVIEWED**

The mutagenicity of **toluene** was evaluated in a dominant lethal assay using three groups of male CD-1 mice (12/group) receiving whole body exposures to nominal concentrations of test material at 0, 100 or 400 ppm for 6 hrs/day, 5 days/week for 8 weeks. Following exposure, each male was mated with two untreated females/week for two consecutive weeks. Females were sacrificed 14 days after the midweek of mating. There was no effect of treatment for all dosed male mice as indicated by mortality, body weight and in-life physical observations. There were no significant differences between treated and control females with respect to fertility indices, average number of implants/pregnant female, average number of dead implants/pregnant female, and proportions of female with one or more dead implants.
[Litton Bionetics, Inc.; Mutagenicity Evaluation of Toluene, Mouse Dominant Lethal Assay, Final Report. (1981), EPA Document No. FYI-AX-1081-0136, Fiche No. OTS0000136-0] **UNREVIEWED**

The ability of **toluene** to cause chromosome aberrations in the bone marrow cells of male Charles River rats exposed by intraperitoneal injection at dose levels of 0, 0.025, 0.082 or 0.247 cc/kg (in DMSO solvent, 0.65 cc/rat/day), either once in an acute study (15 rats/group) or once each day for 5 days in a subchronic study (5 rats/group) was evaluated. Five rats/group in the acute study were sacrificed 6, 24 or 48 hrs following dosing and the rats in the subchronic study were sacrificed 6 hrs after administration of the last dose. 50 cells/animal were scored for chromosome aberrations. None of the cells from any of the treated animals exhibited a significant increase in the frequency of chromosome aberrations.
[Litton Bionetics, Inc.; Mutagenicity Evaluation of Toluene. (1978), EPA Document No. 878210352, Fiche No. OTS0205936] **UNREVIEWED**

The percutaneous absorption of **toluene** was evaluated in six human volunteers. A glass ring having an area of 13cm(2) was placed against the palm and 2ml of 14C-**toluene** was applied. After one minute the ring was removed and adherent liquid allowed to evaporate. All urine was collected and analyzed for radioactive content until background levels of activity were approached. **Toluene** absorption was very low, averaging .022ul/cm(2) for the six human subjects.
[Thomas J. Franz M.D.; Absorption of Petroleum Products Across the Skin of Man and Monkey, Draft Report, (no date), EPA Document No. FYI-AX-0187-0185, Fiche No. OTS0000185-4] **UNREVIEWED**

TOLUENE

CASRN: 108-88-3

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Non-Human Toxicity Excerpts:

A TEMPORARY INCOORDINATION WITH MUSCULAR TREMORS HAS BEEN OBSERVED IN PUPPIES & KITTENS & IN DOGS AT TWICE THERAPEUTIC DOSE LEVEL. CALVES IN POOR CONDITION SHOWED STAGGERING GAIT AND SOME COLLAPSED BUT RECOVERY WAS COMPLETE AFTER UP TO 4 HOURS. FOUR TIMES THERAPEUTIC DOSE RATE PRODUCED NO OBSERVABLE CHANGES IN ... ORGANS.
[Clarke, M. L., D. G. Harvey and D. J. Humphreys. Veterinary Toxicology. 2nd ed. London: Bailliere Tindall, 1981. 100]**PEER REVIEWED**

... /CNS DEPRESSANT/ EFFECT OF **TOLUENE** ... IS EXERTED IN 2 PHASES--A PRELIMINARY ... /CNS DEPRESSION/ FOLLOWED BY STAGE OF EXCITEMENT, MANIFESTED BY TREMOR, MUSCULAR CRAMPS AND DISTURBANCES IN BEHAVIOR ...
[Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965. 70]**PEER REVIEWED**

... SWELLING OF GLOMERULI, CYLINDERS & ALBUMIN IN URINE IN 2 ... DOGS. BUT ... /INVESTIGATORS/ NOTE THAT THE DOGS WERE OF BREED WHICH FREQUENTLY DEVELOP INTERSTITIAL NEPHRITIS. ... HEMORRHAGIC & DEGENERATIVE LESIONS IN GOATS.
[Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965. 72]**PEER REVIEWED**

IN DOGS ... CONGESTION & HEMORRHAGIC FOCI WERE PRESENT IN LIVER; THESE LESIONS ... ALSO PRESENT IN GOATS ... CONGESTION & SOME ALVEOLAR INFLAMMATION /OF LUNG ALSO/ ... IN DOGS & ... GOATS. SPLEEN ... SHOWED SOME DIMINUTION OF LYMPHOID FOLLICLES & PLAQUES OF HEMOSIDEROSIS.
[Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965. 71]**PEER REVIEWED**

EFFECTS IN CATS EXPOSED TO 7800 PPM (31.0 MG/L)/6 HR: CNS EFFECTS, MYDRIASIS, MILD TREMORS, PROSTRATION IN 80 MIN, LIGHT ANESTHESIA IN 2 HR. /FROM TABLE/
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1327]**PEER REVIEWED**

INTRATRACHEAL ADMIN /TO CATS/ WITH CHRONICALLY IMPLANTED ELECTRODES INDUCED SEIZURES ALONG WITH BEHAVIORAL DISTURBANCES SUCH AS NODDING, TWITCHING & APPARENT HALLUCINATIONS.
[CONTRERAS CM ET AL; ELECTROENCEPHALOGR CLIN NEUROPHYSIOL 46 (3): 290 (1979)]**PEER REVIEWED**

... RATS /EXPOSED/ TO 1500 MG/CU M OF AIR FROM DAY 1 THROUGH 8 OR 1000 MG/CU M

FOR 8 HR DAILY FROM DAY 1 THROUGH DAY 21 /OF GESTATION/ ... /WITH/ NO TERATOGENIC EFFECT. SOME FETAL GROWTH RETARDATION ... @ HIGHER DOSE ... MICE WERE EXPOSED DURING DAYS 6-13 TO 1500 MG/CU M OF AIR WITH SIMILAR RESULTS.
[Shepard, T.H. Catalog of Teratogenic Agents. 5th ed. Baltimore, MD: The Johns Hopkins University Press, 1986. 1438]**PEER REVIEWED**

/GAVAGING/ MICE /WITH/ 1.0 MG/KG ON DAYS 6 THROUGH 15 /OF GESTATION/ ... INCR CLEFT PALATE IN THE OFF-SPRING.
[Shepard, T.H. Catalog of Teratogenic Agents. 5th ed. Baltimore, MD: The Johns Hopkins University Press, 1986. 1438]**PEER REVIEWED**

TOLUENE WAS UNABLE TO REVERT SALMONELLA TYPHIMURIUM STRAINS TA1535, TA1537, TA1538, TA98 AND TA100 IN THE AMES SALMONELLA/MICROSOME ASSAY, EITHER WITH OR WITHOUT METABOLIC ACTIVATION BY S9 MIX FROM LIVERS OF RATS EITHER UNTREATED OR INDUCED WITH AROCLOR 1254.
[BOS RP ET AL; MUTAT RES 88: 273 (1981)]**PEER REVIEWED**

FOLLOWING IP ADMIN OF 1 ML **TOLUENE**/KG DAILY FOR 21 DAYS TO RATS, MIXED-FUNCTION OXYGENASE ACTIVITY INCREASED 33.8% IN LIVER BUT WAS UNCHANGED IN BRAIN.
[CHAND P, CLAUSEN J; BULL ENVIRON CONTAM TOXICOL 28 (5): 542 (1982)]**PEER REVIEWED**

TOLUENE & M-XYLENE CAUSED MUSCULAR WEAKNESS & EQUILIBRIUM DISTURBANCES IN THE RAT FOLLOWING IP ADMIN. THE LOCOMOTOR (OPEN-FIELD BEHAVIOR) & RUNNING ACTIVITY (WHEEL-RUNNING) IN THE RAT WAS MOST AFFECTED BY **TOLUENE**. THESE DIFFERENCES WERE RELATED TO THE DIFFERENCES IN THE STIMULATORY EFFECTS OF THE SOLVENTS ON THE CNS.
[PAKSY KA ET AL; ACTA PHYSIOL ACAD SCI HUNG 59 (4): 317 (1982)]**PEER REVIEWED**

RATS WERE EXPOSED TO **TOLUENE** OR N-HEXANE OR A MIXT OF THE 2 CMPD AT 1000-8000 PPM FOR 8 HR. ACETYLCHOLINE WAS INCR AT LOW CONCN OF THE SOLVENTS, BUT WAS GREATLY DECR AT HIGH CONCN. CHOLINE ACETYLTRANSFERASE WAS DECR SIGNIFICANTLY AT HIGH CONCN OF THE MIXT. ACETYLCHOLINE ESTERASE ACTIVITY WAS INCR BY THE SOLVENTS.
[HONMA T; TOXICOL LETT 16 (1-2): 17 (1983)]**PEER REVIEWED**

In skin painting studies with CF1, CH, and BaH strains of mice, 0.05 to 0.1 ml/mouse was applied to 25 mice/sex/strain for 52 weeks. Results were negative for tumor development.
[USEPA; Ambient Water Quality Criteria Doc: Toluene p.C-26 (1980) EPA 440/5-80-075]**PEER REVIEWED**

Intraperitoneal admin of 250, 500, or 1,000 mg/kg at 0 and 24 hr failed to give positive results in micronucleus test with Swiss mice.
[USEPA; Ambient Water Quality Criteria Doc: Toluene p.14-6 (1980) EPA 440/5-80-075]**PEER REVIEWED**

... Groups of rats were trained on the conditioned avoidance response task during the last week of a 5 week exposure to 1400 or 1200 ppm **toluene** (14 hr/day, 7 days/week) or during the first or third weeks after the exposure ended. None of the three groups ... were able to acquire the auditory condition avoidance response ... . Subsequent tests ... revealed that hearing with these rats was unimpaired at 4 KHz, slightly impaired at 8 KHz, and markedly impaired at 12 KHz and above.
[Pryor GT et al; Neurobehav Toxicol Terat 5 (1): 53-7 (1983)]**PEER REVIEWED**

Pregnant CD-1 mice were housed singly in multicompartment cages in inhalation chambers and exposed to **toluene** at a concentration of 0, 750, or 1500 mg/cu m (0, 200, or 400 ppm) for 7 hrs/day from day 7 through day 16 of gestation. The mice were killed on day 17 of gestation and the fetuses were removed and examined. Maternal weight gain was not affected by **toluene** exposure but the liver to body weight ratio was significantly reduced. The treated dams showed no significant differences in the average number of implantation sites, number of live fetuses, fetal mortality, or fetal body weight at either **toluene** concentration compared to control values. The incidence of enlarged renal pelvis was significantly greater in fetuses exposed to 200 ppm than in the fetuses exposed to 400 ppm or in the controls. A shift in rib profile (number of fetuses with 13 ribs) was observed in the higher **toluene** concentration group, and this shift was significantly different from the rib profile of controls. There was an increase in the total activity of lactic dehydrogenase activity in the brain of the dams from the 400 ppm group. The total activity of lactic dehydrogenase in the **toluene** exposed pups did not differ significantly from the controls for liver, heart, lung, or kidney, but the brain lactic dehydrogenase activity of the treated group was slightly greater than the control value.
[Courtney KD et al; Fundam Appl Toxicol 6: 145-54 (1986)]**PEER REVIEWED**

Behavioral toxicity of **toluene** was assessed in mice confined in a 20 liter hermetically sealed chamber for several hours. **Toluene** was introduced through a port and volatilized by a hot plate. Samples of chamber air for analysis were taken through another port. A smaller mesh cage held the mouse within the larger chamber. Schedule-controlled responding was developed by arranging that a response, breaking a beam of light, was followed by mild (under an F1 60 sec) schedule. Responding was much more rapid in the presence of stimuli correlated with the F1 schedule than when the schedule was not operating. Standard sessions consisted of alternating series of 8 consecutive F1 60 sec and inter-series 30 min time-outs. Concentration-effect curves were determined by exposing a mouse to incremental additions of **toluene** at 30 min intervals. **Toluene** increased the rate of responding in most mice at levels of about 700 ppm. Higher concentrations progressively reduced responding. The ED50 (the concentration reducing responding by 50%) averaged 1657 ppm in 10 mice. It is estimated that there is a 1/1000 chance /ED001/ of the responding of a mouse being reduced by as much as 10% by a concentration of **toluene** of 69 ppm.
[Glowa JR et al; J Environ Pathol Toxicol Oncol 6 (5-6): 153-68 (1986)]**PEER REVIEWED**

Sixteen rats were chronically implanted with bipolar electrodes in the hipocampal regions containing cells generating electric theta-activity. The animals were divided into 4 groups of which 2 were exposed to 500 ppm of **toluene** in inhalation chambers, for 8 or 16 hours per day for 5 days per week in 12 weeks respectively, and 2 served as controls. The hippocampal electric activity was recorded 48 hours after each weekly exposure. Frequencies of theta-activity in the exposed groups were found to differ from their respective control group by variance analysis. Each point on the frequency versus time plot were further analysed by Student's t-test. Compared to the non-exposed group the eight hours daily exposed

showed an initial period of increased frequency of the regular theta-waves together with an increased incidence of theta-activity after 1-2 weeks of exposure. In the sixteen hours daily exposed rats two weeks of **toluene** inhalation produced a significant reduction in the theta-wave frequency. This change was also reached after either weeks of exposure in the eight hours daily exposed group. At this moment the theta-activity was frequency disrupted by short amplitude irregular waves, a phenomen which increased gradually throughout the rest of the exposure period. The average blood concentration of **toluene** was 16.7 ug/ml and 17.7 ug/ml and not significantly different for the eight and sixteen hours exposed groups respectively.
[Naalsund LU; Acta Pharmacol Toxicol 59 (4): 325-31 (1988)]**PEER REVIEWED**

The effects of **toluene** vapors on brain lipid changes were investigated in male Sprague-Dawley rats. The animals (8/group) were continuously exposed to 320 ppm **toluene** for 30 days. Controls were exposed to air. Exposed animals showed decreased body weight ($p< 0.01$), decreased brain weight ($p< 0.01$), and a decrease in the weight of the cerebral cortex ($p< 0.05$) when compared to controls. In the cerebral cortex of exposed rats, total phospholipids was reduced ($p< 0.001$), there was an increase in phosphatidic acid ($p< 0.05$) and a decrease in a minor fatty acid of ethanolamine phosphoglyceride ($p< 0.05$). No changes in lipids were found in the brain stem.
[Kyrklund T et al; Toxicology 45: 123-33 (1987)]**PEER REVIEWED**

With the intention of investigating possible morphological alterations effected by **toluene** in the developing CNS, rat pups were exposed to 100 ppm and 500 ppm of atmospheric **toluene** from postnatal day 1 until sacrifice at postnatal day 28, when the hippocampal region (area dentata, Ammon's horn, subiculum) was examined by light microscope and alterations in the volumes of the layers of the subdivisions were determined. The layers of Ammon's horn and the subiculum were not affected qualitatively or quantitatively by the 500 ppm exposure. Within the area dentata, the volume of the granule cell layer was 6% smaller in animals exposed to 100 ppm and 13% smaller in animals exposed to 500 ppm than they were in controls. The volumes of the hilus, which is a terminal field of granule cell axons, and the commissural-association zone of the dentate molecular layer, which is the terminal field of the hilar projection to the granule cells, were smaller (12% and 19%) in animals exposed to 500 ppm than they were in controls. Argyrophilic cells were found in the granule cell layer of all animals exposed to 500 ppm. Pronounced granule cell degeneration was found in one animal exposed to 500 ppm. The granule cell layer of animals exposed to 100 ppm appeared qualitatively normal. The alterations reported here support the few earlier reports of morphological alterations in the CNS of adult laboratory animals. Effects of **toluene** similar to those described, that is alterations in specific neuron populations and their afferent and efferent terminal fields may complement changes in neurophysiology and behavior that have been observed in prenatally and perinatally exposed rodent pups. Causal relationships, however, remain to be elucidated.
[Slomianka L et al; Toxicol 62 (2): 189-202 (1990)]**PEER REVIEWED**

The aim of the present study was to investigate the effects of **toluene** on fetal development in well nourished and malnourished rats. Long-term behavioral consequences after in utero exposure were also studied. **Toluene** (1.2 g/kg sc) was administered daily to well nourished and to malnourished (food restricted to 50% of ad libitum intake) pregnant rats, during the second (8-15 days) or the third week of pregnancy (14-20 days). Offspring were evaluated for malformation, development of the skeleton, prenatal growth of the brain and liver, postnatal growth and long lasting behavioral effects. In utero exposure to **toluene** during the third week of pregnancy resulted in low body weight at birth, which

persisted in the male offspring into adulthood. Malnutrition increased fetal susceptibility to the effects of **toluene** as indicated by evaluation of the development of the skeleton. Behavioral tests performed when the pups were 30 and 90 days old showed effects of in utero malnutrition (increased ambulation and worse performance in a shuttle box), but no behavioral effects related to **toluene** exposure were detected. These data indicate that in utero exposure to **toluene** can have long lasting effects on body growth and that maternal malnutrition increases the risk for **toluene** fetotoxicity.
[Silva V AD et al; Toxicol 64 (2): 155-68 (1990)]**PEER REVIEWED**

Toluene did not induce gene mutations in Salmonella typhimiurium strain TA98, TA100, TA1535, or TA1537 with or without exogenous metabolic activation. In the mouse lymphoma assay, **toluene** gave an equivocal response with and without exogenous metabolic activation. **Toluene** did not induce sister chromatid exchanges or chromosomal aberrations in Chinese hamster ovary cells in the presence or absence of exogenous metabolic activation.
[DHHS/NTP; Toxicology and Carcinogenesis Studies of Chlorobenzene in F344/N Rats and B6C3F1 Mice (Inihalation Studies) p.4 (1990) Technical Rpt Series No. 371 NIH Pub No. 90-2826]**PEER REVIEWED**

... **Toluene** can alter learned behavior at concentrations below anesthetic levels but, in general, above 1000 ppm.
[Klaassen, C.D., M.O. Amdur, Doull J. (eds.). Casarett and Doull's Toxicology. The Basic Science of Poisons. 5th ed. New York, NY: McGraw-Hill, 1995. 747]**PEER REVIEWED**

Toluene was injected into the yolk sac of fresh fertile chicken eggs prior to incubation. Hatchability of the eggs was 85%, 25%, and 0 with exposures of 4.3, 8.7, and 17.4 mg/egg, respectively.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47 96 (1989)]**PEER REVIEWED**

Toluene was reported to induce chromosomal aberrations in the bone marrow cells of male albino rats after chronic inhalation exposure to 5.4 or 50.7 mg/cu m on 4 hr/day, five days/wk for four months or after sc injection of 0.8 g/kg bw. Chromosomal aberrations in bone marrow cells were reported following sc injection of 1 g/kg bw daily for 12 days to male albino rats.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47 98 (1989)]**PEER REVIEWED**

Toluene and benzene administered concurrently were reported to have an additive effect on induction of chromosomal aberrations. **Toluene** reduced the number of sister chromatid exchanges induced by benzene when both compounds were administered intraperitoneally to DBA/2 mice and reduced the clastogenic activity of benzene when the two compounds were simultaneously administered orally to CD-1 mice, intraperitoneally to Sprague-Dawley rats, or subcutaneously to NMRI mice.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47

99 (1989)]**PEER REVIEWED**

Animal studies in mice exposed to **toluene** at concentrations of 2.5-500 ppm demonstrated decreased host defense to respiratory infections.
[Sullivan, J.B. Jr., G.R. Krieger (eds.). Hazardous Materials Toxicology-Clinical Principles of Environmental Health. Baltimore, MD: Williams and Wilkins, 1992. 1092]**PEER REVIEWED**

The cardiovascular response of 25 mongrel dogs following exposure to 30,000 ppm **toluene** for 9-10 min was complex. For most of the animals, there was no change in electrocardiogram readings for the first 3-4 min of exposure. The heartbeat then became rapid for several minutes, and was followed by a period of bradycardia. Immediately before death ventricular fibrillation was noted. ... Four of the dogs were particularly sensitive, their ventricular arrhythmias were transient and accompanied by fluctuations of blood pressure. The authors suggested that **toluene** had a direct effect on the septal and ventricular muscles of the heart which permitted the development of fatal arrhythmias in sensitive dogs.
[Ikeda N et al; Forensic Sci Intern 44: 151-8 (1990) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.31 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

Mice exposed for 3 hr to **toluene** at concentrations of 2.5-500 ppm exhibited increased, but not dose-related, susceptibility to respiratory infections when challenged by Streptococcus zooepidemicus. Pulmonary bactericidal activity was decreased at concentrations of 2.5 ppm and 100-500 ppm but not at concentrations of 5-50 ppm. There was no effect on susceptibility to infection with a **toluene** exposure of 1 ppm for 3 hr, 5 days (3 hr/day) or 4 wk (3 hr/day). The bactericidal activity of the lung was decreased during the 5-day treatment but not with the 4-wk treatment. The authors hypothesized that **toluene** exerted an adverse effect on alveolar macrophage function, thereby decreasing disease resistance.
[Aranyi C et al; Toxicol Lett 25: 103-10 (1985) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.39 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

Studies have demonstrated that **toluene** can produce subtle changes in the auditory system. Intermediate exposure to **toluene** produced a permanent loss of hearing in the high frequency range (approximately 16 kHz) in rats exposed to 1200 ppm for 5-9 wk or 1000 ppm for 2 wk.
[Pryor GT, Rebert CS; Neurotoxicology 13: 225-34 (1992) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.44 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

In 3-day-old rats, daily 15 min exposures to **toluene** resulted in a dose-related increase in righting-reflex latency time. At each dose the righting-reflex latency decreased over the first 4 wk of exposure indicating that the animals had developed at least partial tolerance to the **toluene**. During the second 4-wk period, latencies increased again at the higher doses but were never as great as they were for the initial **toluene** exposure. The results for the second 4-wk period showed that there were limitations to the adaptive response at the higher **toluene** doses and that there were cumulative effects of exposure at these doses. Tolerance was probably the result of induction of **toluene** metabolizing enzymes.

[Lorenzana-Jimenez M, Salas M; Neurotoxicol Teratol 12: 353-7 (1990) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.45 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

Concentrations of 480 ppm and above decreased the ability of trained rats to perform a sequence of lever press actions associated with a reward (milk). During training, the rats were divided into two groups. The reward presentation for one group was not accompanied by any noticeable external events. For the second group, the reward presentation was accompanied by light and sound stimuli. The effects of **toluene** on performance were less severe with the rats trained using the light and sound reinforcement. This suggests that behavior associated with external signals is less subject to disruption by **toluene** than behavior that is not accompanied by external reinforcement.
[Wood RW et al; Toxicol Appl Pharmacol 68: 462-72 (1983) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.45 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

Age ... influences neurological response after exposure to **toluene**. Young rats (50 days old) were affected by **toluene** to a lesser extent than older rats (120 days old) based on several measurements of escape latency 30 days after exposure to 30,000-40,000 ppm for 15 min/day.
[Castilla-Serna L et al; Arch Invest Med 22: 295-301 (1991) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.46 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

Toluene exposure ... changes sleep patterns in animals. Both single episodes of **toluene** exposure (about 1000 ppm) and subchronic 8 hr/day exposures for 3 wk (about 600 ppm), changed patterns of sleep and wakefulness in rats. After the single exposures, there was a decrease in wakefulness and an increase in slow-wave sleep; a prolonged sleep latency was apparent for the 2 days following exposure. Latency was defined as the time interval between the end of the exposure period and the beginning of a particular phase of the sleep cycle. Following the 3 wk exposures, there was an increase in wakefulness during the dark period on the 2 days after exposure and a decrease in slow wave sleep on the first day.
[Arito H et al; Arch Toxicol 62: 76-80 (1988) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.46 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

Brain levels of norepinephrine, dopamine, serotonin, vanillylmandelic acid, homovanillic acid, and 5-hydroxyindolacetic acid were altered in six areas of the brain in male CD-1 mice administered **toluene** (5-105 mg/kg/day) in their drinking water for a 28-day period. Significant increases of norepinephrine, dopamine, and serotonin were present in the hypothalamus at all dose levels. The maximum increase occurred with the 22 mg/kg/day dose and there were lesser increases for both the 5 and 105 mg/kg/day doses, giving biphasic response. Roughly similar fluctuations were seen in the concentrations of vanillylmandelic acid and homovanillic acid, which are metabolites of dopamine and norepinephrine and 5-hydroxyindolacetic acid, a serotonin metabolite. In corpus striatum, the levels of dopamine and serotonin were significantly increased at the two highest doses. The level of vanillylmandelic acid was also increased significantly at the same doses. In the medulla oblongata, the concentrations of

norepinephrine, vanillylmandelic acid, and 5-hydroxyindolacetic acid were significantly increased at the 22 mg/kg/day dose, but not at the other doses, while the levels of serotonin were significantly increased at the 22 and 105 mg/kg/day doses. Norepinephrine concentrations were elevated in the midbrain. ...
[U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.61 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

To identify the frequency range most sensitive to **toluene**-induced auditory damage, the auditory function of adult Long-Evans rats exposed to 1750 ppm of **toluene** (6 h/day, 5 days/week, 4 weeks), was tested by recording auditory-evoked potentials directly from the round window of the cochlea. The present electrocochleographic findings do not support a specific mid- to high-frequency loss of auditory sensitivity. On the contrary, the electrophysiologic data, obtained for audiometric frequencies ranging from 2 to 32 kHz, showed a hearing deficit not only in the mid-frequency region (12-16 kHz), but also in the mid-low-frequency region (3-4 kHz). Actually, the effect of **toluene** was independent of the frequency in our experimental conditions. Histological analysis was consistent with electrophysiologic data because a broad loss of outer hair cells occurred in both mid- and mid-apical coil of the organ of Corti.
[Lataye R et al; Neurotoxicol Teratol 21 (3): 267-76 (1999)]**PEER REVIEWED**

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National Toxicology Program Studies:

Long-term studies were conducted by exposing groups of 60 rats /F344/N/ of each sex to 0, 600, or 1,200 ppm **toluene** by inhalation, 6.5 hours per day, 5 days per week. Groups of 60 /B6C3F1/ mice of each sex were exposed at 0, 120, 600, or 1,200 ppm on the same schedule. ... Animals were exposed to **toluene** for 103 weeks. Nephropathy was seen in almost all rats, and the severity was somewhat increased in exposed rats. A rare renal tubular cell carcinoma in a female rat and an equally uncommon sarcoma of the kidney in another female rat were seen in the 1,200 ppm exposure group. Erosion of the olfactory epithelium and degeneration of the respiratory epithelium were increased in exposed rats. Inflammation of the nasal mucosa and metaplasia of the olfactory epithelium were increased in exposed female rats. A rare squamous cell carcinoma of the nasal mucosa was seen in one female rat at 1,200 ppm. A squamous cell papilloma of the forestomach was observed in one female rat at 1,200 ppm, and a squamous cell carcinoma was observed in a second female rat at 1,200 ppm. No chemically related neoplasms were found in male rats, and the one nasal, two kidney, and two forestomach neoplasms observed in female rats were considered not to be associated with inhalation exposure to **toluene**. For mice, no biological important increases were observed for any nonneoplastic or neoplastic lesions.
[DHHS/NTP; Toxicology and Carcinogenesis Studies of Chlorobenzene in F344/N Rats and B6C3F1 Mice (Inhalation Studies) p.4 (1990) Technical Rpt Series No. 371 NIH Pub No. 90-2826]**PEER REVIEWED**

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Non-Human Toxicity Values:

LD50 Rat oral 2.6 to 7.5 g/kg

[DHHS/NTP; Toxicology and Carcinogenesis Studies of Chlorobenzene in F344/N Rats and B6C3F1 Mice (Gavage Studies) p.16 (1990) Technical Rpt Series No. 371 NIH Pub No. 90-2826]**PEER REVIEWED**

LD50 Rabbit dermal 14.1 ml/kg

[DHHS/NTP; Toxicology and Carcinogenesis Studies of Chlorobenzene in F344/N Rats and B6C3F1 Mice (Gavage Studies) p.16 (1990) Technical Rpt Series No. 371 NIH Pub No. 90-2826]**PEER REVIEWED**

LD50 Rat (female) ip 1.64 g/kg

[DHHS/NTP; Toxicology and Carcinogenesis Studies of Chlorobenzene in F344/N Rats and B6C3F1Mice (Inhalation Studies) p.16 (1990) Technical Rpt Series No. 371 NIH Pub No. 90-2826]**PEER REVIEWED**

LD50 MOUSE IP 1.15 G/KG

[KOGA K, OHMIYA Y; J TOXICOL SCI 3 (1): 25 (1978)]**PEER REVIEWED**

LD50 Rat oral 5000 mg/kg

[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 3190]**PEER REVIEWED**

LD50 Rat ip 1332 mg/kg

[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 3190]**PEER REVIEWED**

LD50 Rat iv 1960 mg/kg

[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 3190]**PEER REVIEWED**

LC50 Mouse ihl 400 ppm/24 hr

[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 3190]**PEER REVIEWED**

LD50 Mouse ip 59 mg/kg

[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 3190]**PEER REVIEWED**

LD50 Mouse sc 2250 mg/kg
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 3190]**PEER REVIEWED**

LD50 Mouse ip 640 mg/kg
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 3190]**PEER REVIEWED**

LD50 Rabbit skin 12,124 mg/kg
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 3190]**PEER REVIEWED**

... The LC50 for **toluene** in mice is 5320 ppm/8 hr /via inhalation/ ...
[Klaassen, C.D., M.O. Amdur, Doull J. (eds.). Casarett and Doull's Toxicology. The Basic Science of Poisons. 5th ed. New York, NY: McGraw-Hill, 1995. 746]**PEER REVIEWED**

As the duration of **toluene** inhalation exposure increased, the LC50 in rats decreased from 26,700 ppm for 1 hr, to 12,200 ppm for 2-2.5 hr, to 8000 ppm for 4 hr.
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Volumes I,II, III. Cincinnati, OH: ACGIH, 1991. 1568]**PEER REVIEWED**

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Ecotoxicity Values:

LC50 FOR BLUEGILL WAS 17 MG/L/24 HR & 13 MG/L/96 HR (95% CONFIDENCE LIMIT 11-15 MG/L) @ 21-23 DEG C AFTER EXPOSURE TO **TOLUENE**. /CONDITIONS OF BIOASSAY NOT SPECIFIED/

[BUCCAFUSCO RJ ET AL; BULL ENVIRONM CONTAM TOXICOL 26 (4): 446-52 (1981)]**PEER REVIEWED**

LC50 Palaemonetes pugio (grass shrimp) 9.5 mg/l/96 hr /Conditions of bioassay not specified/

[Verschueren, K. Handbook of Environmental Data on Organic Chemicals. 3rd ed. New York, NY: Van Nostrand Reinhold Co., 1996. 1727]**PEER REVIEWED**

LC50 Cancer magister (crab larvae stage I) 28 mg/l/96 hr /Conditions of bioassay not specified/

[Verschueren, K. Handbook of Environmental Data on Organic Chemicals. 3rd ed. New York, NY: Van Nostrand Reinhold Co., 1996. 1727]**PEER REVIEWED**

LC50 Crangon franciscorum (shrimp) 4.3 mg/l/96 hr /Conditions of bioassay not specified/

[Verschueren, K. Handbook of Environmental Data on Organic Chemicals. 3rd ed. New York, NY: Van Nostrand Reinhold Co., 1996. 1728]**PEER REVIEWED**

LC50 Pimephales promelas (fathead minnow) 56-34 mg/l/24-96 hr /Conditions of bioassay not specified/

[Verschueren, K. Handbook of Environmental Data on Organic Chemicals. 3rd ed. New York, NY: Van Nostrand Reinhold Co., 1996. 1728]**PEER REVIEWED**

LC50 Lebistes reticulatus (guppy) 63-59 mg/l/24-96 hr /Conditions of bioassay not specified/

[Verschueren, K. Handbook of Environmental Data on Organic Chemicals. 3rd ed. New York, NY: Van Nostrand Reinhold Co., 1996. 1729]**PEER REVIEWED**

LC50 Channel catfish 240 mg/l 96 hr /Conditions of bioassay not specified/

[Environment Canada; Tech Info for Problem Spills: Toluene p.71-75 (1981)]**PEER REVIEWED**

LC50 Pimephales promelas (fathead minnow) 34.27 mg/l 96 hr (95% Confidence Limits= 22.83-45.86 mg/l) /Conditions of bioassay not specified/

[Pickering QH, Henderson C; J Water Pollution Control Fed 38: 1419-1429 (1966) as cited in NRC; Alkyl Benzenes p.352 (1981)]**PEER REVIEWED**

LC50 Carassius auratus (goldfish) 57.68 mg/l 96 hr (95% Confidence Limits= 48.87-68.75 mg/l) /Conditions of bioassay not specified/

[Pickering QH, Henderson C; J Water Pollution Control Fed 38: 1419-1429 (1966) as cited in NRC; Alkyl Benzenes p.352 (1981)]**PEER REVIEWED**

LC50 Lebistes reticulatus (guppy) 59.30 mg/l 96 hr (95% Confidence Limits= 50.87-70.34 mg/l) /Conditions of bioassay not specified/
[Pickering QH, Henderson C; J Water Pollution Control Fed 38: 1419-1429 (1966) as cited in NRC; Alkyl Benzenes p.352 (1981)]**PEER REVIEWED**

LC50 Daphnia magna, (water flea) 313 mg/l 48 hr /Conditions of bioassay not specified/
[USEPA. In Depth Studies on Health and Environ Impact of Sel Water Poll (1978) EPA 68-01-4646 as cited in NRC; Alkyl Benzenes p.356 (1981)]**PEER REVIEWED**

LC50 Nitocra spinipes (copepod) 24.2-74.2 mg/l 24 hr /Conditions of bioassay not specified/
[Potera GT; Effects of Benzene, Toluene, and Ethylbenzene on Several Important Members of the Estuarine Ecosystem Ph.D. Dissertation p.1-117 (1975) as cited in NRC; Alkyl Benzenes p.355 (1981)]**PEER REVIEWED**

LC50 Artemia salina (brine shrimp) 33 mg/l 24 hr /Conditions of bioassay not specified/
[Price KS et al; J Water Pollut Control Fed 46: 63-77 (1974) as cited in NRC; Alkyl Benzenes p.355 (1981)]**PEER REVIEWED**

LC50 Morone saxatilis (striped bass) 7.3 mg/l 96 hr /Conditions of bioassay not specified/
[Benville PE, Korn S; Calif Fish Game 63: 204-209 (1977) as cited in NRC; Alkyl Benzenes p.353 (1981)]**PEER REVIEWED**

LC50 Cyprinodon variegatus (sheepshead minnow) 277-485 mg/l 96 hr /Conditions of bioassay not specified/
[NRC; Alkyl Benzenes p.354 (1981)]**PEER REVIEWED**

LC50 Aedes aegypti-4th instar (mosquito larvae) 22 mg/l /Conditions of bioassay not specified/
[USEPA. In Depth Studies on Health Environ Impact of Sel Water Pollutants (1978) EPA 68-01-4646 as cited in NRC; Alkyl Benzenes p.362 (1981)]**PEER REVIEWED**

LC50 Calandra granaria (grain weevil) 210 mg/l /in air/
[Ferguson J, Pirie H; Ann Appl Biol 35:532-550 (1948) as cited in NRC; Alkyl Benzenes p 362 (1981)]**PEER REVIEWED**

LC50 Pimephales promelas (fathead minnows) 55-72 mg/l (embryos), 25-36 mg/l (1-day posthatch protolarvae), and 26-31 mg/l (30-day-old minnows)/ 96 hour /Conditions of bioassay not specified/
[Devlin EW et al; Bull Environ Contam Toxicol 29 (1): 12-17 (1982)]**PEER REVIEWED**

EC50 Pimephales promelas (fathead minnow) 14.6 mg/l/96 hr (confidence limit 14.0 to 15.1 mg/l), flow-through bioassay with measured concentrations, 24.7 deg C, dissolved oxygen 6.9 mg/l, hardness

45.4 mg/l calcium carbonate, alkalinity 43.4 mg/l calcium carbonate, and pH 7.89. Effect: loss of equilibrium.
[Geiger D.L., Poirier S.H., Brooke L.T., Call D.J., eds. Acute Toxicities of Organic Chemicals to Fathead Minnows (Pimephales Promelas). Vol. III. Superior,Wisconsin: University of Wisconsin-Superior, 1986. 163]**PEER REVIEWED**

LC50 Pimephales promelas (fathead minnow) 36.2 mg/l/96 hr (confidence limit 29.4 to 44.6 mg/l), flow-through bioassay with measured concentrations, 24.7 deg C, dissolved oxygen 6.9 mg/l, hardness 45.4 mg/l calcium carbonate, alkalinity 43.4 mg/l calcium carbonate, and pH 7.89.
[Geiger D.L., Poirier S.H., Brooke L.T., Call D.J., eds. Acute Toxicities of Organic Chemicals to Fathead Minnows (Pimephales Promelas). Vol. III. Superior,Wisconsin: University of Wisconsin-Superior, 1986. 163]**PEER REVIEWED**

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TSCA Test Submissions:

Neurotoxicity was determined in groups of rats (4 male and 4 female, strain not reported) exposed by inhalation to 0,100, or 1500 ppm **toluene** (purity not reported) 6 hrs/day, 5 days/week for periods up to 27 weeks. Histological sections of selected areas of the brainstem were made for the upper medulla oblongata (including dorsal and ventral cochlear and vestibular nuclei), lower metencephalon (including superior olivary nuclei, trapezoid body and ventral cochlear nuclei), upper metencephalon (including the lateral lemniscus, superior olivary nuclei, cochlear and vestibular nuclei, and inferior colliculus) and the mesencephalon-diencephalon junction (including the medial geniculate). The investigators reported that the "vast majority" of sections from animals exposed to **toluene** were indistinguishable from controls. Shrunken and darkly stained neurons were observed in the corpus trapezoid of one animal exposed to 100 ppm and another exposed to 1500 ppm **toluene**; these were present in only one section and not in sufficient quantity to be considered a positive response by the investigators. Statistical analysis of the results was not reported.
[American Petroleum Inst.; Effects of Toluene Exposure on Auditory Pathways, Final Report. (1979), EPA Document No. 40-8450019, Fiche No. OTS0507495] **UNREVIEWED**

Chronic toxicity was evaluated in male and female Sprague Dawley rats (15/sex/group) exposed to **toluene** via inhalation at 0, 100 and 1500 ppm for 6 hrs/day, 5 days/week for 26 weeks. There were significant increases in the hematocrit and hemoglobin levels in females at 1500 ppm in the 13th week. There were significant differences in females at week 26 in the following: decreased mean blood clotting time and increased mean serum glutamic pyruvic transaminase at 100 ppm level, and decreases in glucose levels at 1500 ppm. There were no significant differences between treated and control animals in urinalysis.
[American Petroleum Institute; 26 Week Inhalation Toxicity Study in the Rat (1980), EPA Document No. FYI-AX-1081-0136, Fiche No. 0136-0] **UNREVIEWED**

Teratogenicity was evaluated in mated female CRL:COBS CD (SD) BR rats (27/group) exposed to **toluene** by inhalation at nominal concentrations of 0, 100 or 400 ppm on gestation days (GD) 6-15 for 6 hrs/day. The adult female rats were sacrificed on GD 20 and examined. There were no significant differences observed between treated and control animals in the following: maternal mortality, body weights, food consumption, examination of tissues and organs at necropsy (except an insignificant number of observations of mottled lungs in 4 high-dose group rats), pregnancy rate, live litters, implantation sites, resorptions, litters with resorptions, dead pups, litters with dead pups, live pups/implantation site, mean live litter size, average pup weights, fetal sex ratio, examination of soft tissues of the head, thoracic and visceral organs, and skeletal abnormalities.
[Litton Bionetics, Inc.; Teratology Study in Rats, Toluene, Final Report (1978), EPA Document No. 87-8210353, Fiche No. OTS0205936] **UNREVIEWED**

The ability of **toluene** to induce specific locus mutations at the TK locus in cultured L5178Y mouse

lymphoma cells (Mouse Lymphoma Mutagenesis Assay) was evaluated in the presence and absence of mouse liver S9 metabolic activation. Based on preliminary toxicity tests, both nonactivated and S9-activated cultures were treated with 0.30, 0.20, 0.15, 0.10, or 0.050 ul/ml produced a range of 7 - 78% total growth for nonactivated cultures and from 60 - 138% total growth for S9-activated cultures. None of the nonactivated or activated cultures produced mutant frequencies significantly greater than the solvent (DMSO) controls.
[Litton Bionetics, Inc.; Mutagenicity Evaluation of Toluene. (1978), EPA Document No. 878210352, Fiche No. OTS0205936] **UNREVIEWED**

The mutagenicity of **toluene** was evaluated in Salmonella tester strains TA98, TA100, TA1535, TA1537 and TA1538, and the yeast Saccharomyces cerevisiae tester strain D4, both in the presence and absence of added metabolic activation by Aroclor-induced rat liver S9 fraction. Based on preliminary bacterial toxicity determinations, **toluene**, diluted with acetone, was tested for mutagenicity at concentrations up to 5.0 ul/plate using both the plate and suspension assay methods. **Toluene** did not cause a positive response in any of the bacterial or yeast tester strains, either with or without metabolic activation.
[Litton Bionetics, Inc.; Mutagenicity Evaluation of Toluene. (1978), EPA Document No. 878210352, Fiche No. OTS0205936] **UNREVIEWED**

The mutagenicity of **toluene** was evaluated in a dominant lethal assay using three groups of male CD-1 mice (12/group) receiving whole body exposures to nominal concentrations of test material at 0, 100 or 400 ppm for 6 hrs/day, 5 days/week for 8 weeks. Following exposure, each male was mated with two untreated females/week for two consecutive weeks. Females were sacrificed 14 days after the midweek of mating. There was no effect of treatment for all dosed male mice as indicated by mortality, body weight and in-life physical observations. There were no significant differences between treated and control females with respect to fertility indices, average number of implants/pregnant female, average number of dead implants/pregnant female, and proportions of female with one or more dead implants.
[Litton Bionetics, Inc.; Mutagenicity Evaluation of Toluene, Mouse Dominant Lethal Assay, Final Report. (1981), EPA Document No. FYI-AX-1081-0136, Fiche No. OTS0000136-0] **UNREVIEWED**

The ability of **toluene** to cause chromosome aberrations in the bone marrow cells of male Charles River rats exposed by intraperitoneal injection at dose levels of 0, 0.025, 0.082 or 0.247 cc/kg (in DMSO solvent, 0.65 cc/rat/day), either once in an acute study (15 rats/group) or once each day for 5 days in a subchronic study (5 rats/group) was evaluated. Five rats/group in the acute study were sacrificed 6, 24 or 48 hrs following dosing and the rats in the subchronic study were sacrificed 6 hrs after administration of the last dose. 50 cells/animal were scored for chromosome aberrations. None of the cells from any of the treated animals exhibited a significant increase in the frequency of chromosome aberrations.
[Litton Bionetics, Inc.; Mutagenicity Evaluation of Toluene. (1978), EPA Document No. 878210352, Fiche No. OTS0205936] **UNREVIEWED**

The percutaneous absorption of **toluene** was evaluated in six human volunteers. A glass ring having an area of 13cm(2) was placed against the palm and 2ml of 14C-**toluene** was applied. After one minute the ring was removed and adherent liquid allowed to evaporate. All urine was collected and analyzed for radioactive content until background levels of activity were approached. **Toluene** absorption was very low, averaging .022ul/cm(2) for the six human subjects.
[Thomas J. Franz M.D.; Absorption of Petroleum Products Across the Skin of Man and Monkey, Draft Report, (no date), EPA Document No.

FYI-AX-0187-0185, Fiche No. OTS0000185-4] **UNREVIEWED**

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Metabolism/Pharmacokinetics:

Metabolism/Metabolites:

Toluene is extensively metabolized via oxidation to benzyl alcohol then to benzaldehyde by alcohol dehydrogenase. Further oxidation then forms benzoic acid. Conjugation with glycine produces the major metabolite, hippuric acid, which is excreted in the urine. Benzyl glucuronide is formed in smaller amounts by conjugation with glucuronic acid.
[Haddad, L.M., Clinical Management of Poisoning and Drug Overdose. 2nd ed. Philadelphia, PA: W.B. Saunders Co., 1990. 1224]**PEER REVIEWED**

IN PRINTERS EXPOSED TO AIR CONTAINING **TOLUENE** (AVG CONCN 23 PPM), URINARY EXCRETION OF O-CRESOL, WHICH IS NOT A NORMAL CONSTITUENT OF URINE, WAS OBSERVED. APPARENTLY, **TOLUENE** WAS OXIDIZED AT AROMATIC NUCLEUS FORMING CRESOLS, BESIDES HIPPURIC ACID.
[ANGERER J; INT ARCH OCCUP ENVIRON HEALTH 43 (1): 63 (1979)]**PEER REVIEWED**

In rats, approx 0.5%-1.1% of the dose is converted to o-cresol and p-cresol and is excreted as glucuronide and sulfate conjugates.
[Bakke OM, Scheline RR; Tox Appl Pharm 16: 691-700 (1970) as cited in NRC; Alkyl Benzenes p.221 (1981)]**PEER REVIEWED**

In mammalian species, acidic metabolites are conjugated with glycine to form hippuric acid and phenylacetic acid. In humans, the phenylacetic acid metabolite is also conjugated with glutamine to form phenacetylglutamine.
[James MO et al; Proc R Soc Lond Ser B 182: 25-35 (1972) as cited in NRC; Alkyl Benzenes p.219 (1981)]**PEER REVIEWED**

The association between occupational **toluene** exposure and blood and adipose tissue **toluene** concentrations was examined. Breathing zone samples were monitored for **toluene** in two Swedish rotogravure printing facilities. Sc adipose tissues were taken from 37 workers after work on Thursday or Friday and analyzed for **toluene**. Venous blood samples were taken from 11 workers after work on Friday and at various times over the following weekend and assayed for **toluene**. Blood and adipose tissue samples were obtained from 11 other workers immediately after work and after 63 and 135 hours nonexposure and analyzed for **toluene**. Blood samples were also taken from 21 unexposed workers and analyzed for **toluene**. Attempts were made to fit the blood **toluene** data to various pharmacokinetics models. Airborne **toluene** concentrations in the printing factories ranged from 8 to 416 mg/cu m, median 75 mg/cu m. Blood **toluene** concentrations in the unexposed workers were below the detection limit, 0.01 umole/l. Blood samples obtained immediately after work contained 0.22 to 21.4 umole/l **toluene**. Elimination of **toluene** from the blood could be described by a three compartment model having median halftimes of 9 minutes, 2 hours, and 79 hours. **Toluene** was eliminated from adipose tissue with a median halftime of 79 hours. Adipose tissue concentrations were significantly associated with the workers'

exposure to airborne **toluene** during the previous week. Adipose tissue **toluene** concentrations were significantly correlated with blood **toluene** concentrations after 70 hours exposure. It was concluded that the prolonged presence of **toluene** in the blood means that there is an endogenous exposure from adipose tissue depots that continues long after occupational exposure has ended.
[Nise G et al; Br J Ind Med 46 (6): 407-11 (1989)]**PEER REVIEWED**

Evidence has suggested that there is an ethnic related difference in organic solvent metabolism in humans; analyses were thus made to obtain evidence of strain differences in animals to assist in consolidating the observation in workers. Female Donryu, Fischer, Sprague-Dawley, and Wistar rats were exposed to **toluene** at dose levels of 5, 45, 500, 2500, and 3500 ppm for 8 hours in a dynamic flow type exposure system. Urine samples were collected for 24 hours from the start of exposure. While the variation in free p-cresol excretion was wide among the rats of the same strain exposed to **toluene** at the same concentration, it was also noted that the four strains tested could be classified into two groups depending on the free p-cresol levels at **toluene** concentrations up to 500 ppm. No significant differences were noted between Sprague-Dawley and Wistar strains nor between Donryu and Fischer strains at the 45 and 500 ppm levels. However, there were significant differences between these two groups. At higher concentrations of 2500 and 3500 ppm, the increase in the free p-cresol levels was remarkable only in Donryu rats, reaching the levels of Sprague-Dawley and Wistar rats, while the level in Fischer rats remained unchanged.
[Inoue O et al; Bull Environ Contam Toxicol 43 (1): 74-9 (1989)]**PEER REVIEWED**

The mutual metabolic suppression between benzene and **toluene** was studied. The subjects, 190 male Chinese workers employed in shoe manufacturing, printing, audio equipment manufacture, and automobile industries, were divided into four groups based on occupational exposure: 65 were exposed to benzene, 35 to **toluene**, 55 to both compounds, and 35 served as comparisons. The arithmetic mean exposure level of benzene was 31.9 and of **toluene** 44.7 ppm. The mixture contained benzene at 17.9 +/29.3 and **toluene** at 20.5 +/25.8 ppm. The exposure levels were measured using individuals diffusive samplers. The geometric mean levels of the metabolites, phenol, catechol, hydroquinone, hippuric acid, and o-cresol, in unexposed workers were 6.9, 9.4, 4.8, 72.5, and 0.066 mg per liter, respectively. Values corrected for creatinine and specific gravity were different from the values cited above. Multiple correlation coefficients for benzene exposure versus its three metabolites were for phenol, 0.740; for catechol, 0.629; and for hydroquinone, 0.726. Multiple correlation coefficients for **toluene** and its two metabolites were 0.649 for hippuric acid and 0.583 for o-cresol. The slopes of regression lines for the exposure to benzene in the presence of **toluene** were less than half of those obtained when the workers were exposed to benzene alone; however, the regression lines for benzene in mixture versus catechol were about 80% or higher than the lines observed with benzene as the sole pollutant. The regression lines for **toluene** in the mixture and excretion level of hippuric acid and o-cresol showed reduced metabolic conversion compared to when exposure was limited to **toluene** alone. It was concluded that simultaneous exposure to benzene and **toluene** results in mutual suppression of metabolism yielding the urinary metabolites phenol, hydroquinone, hippuric acid, and o-cresol.
[Inoue O et al; Int Arch Occup Environ Health 60 (1): 15-20 (1988)]**PEER REVIEWED**

Absorption, Distribution & Excretion:

TOLUENE VAPOR IS READILY ABSORBED BY INHALATION AND THE LIQUID BY THE GI

TRACT, BUT POORLY FROM THE SKIN.
[Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965. 68]**PEER REVIEWED**

IN DOGS SUBJECTED TO INHALATION ... HIGHEST CONCENTRATIONS WERE FOUND IN THE ADRENALS (20 UG/G), BRAIN (19 UG/G IN CEREBELLUM & 18 UG/G IN CEREBRUM), AND BONE MARROW (18 UG/G).
[Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965. 69]**PEER REVIEWED**

ALTHOUGH SOME ABSORBED **TOLUENE** MAY BE REEXHALED BY LUNG, MAJOR EXCRETORY PATHWAY IS RAPID OXIDATION OF **TOLUENE** TO BENZOIC ACID, WHICH IS CONJUGATED WITH GLYCINE & EXCRETED AS HIPPURIC ACID IN URINE. ... WITHIN REASONABLE LIMITS, EXCRETION OF HIPPURIC ACID IN URINE IS PROPORTIONAL TO EXPOSURE. AN EXPOSURE OF 200 PPM OF **TOLUENE** RESULTED IN EXCRETION OF 3.5 G HIPPURIC ACID PER LITER OF URINE (SPECIFIC GRAVITY 1.016).
[Doull, J., C.D. Klaassen, and M. D. Amdur (eds.). Casarett and Doull's Toxicology. 2nd ed. New York: Macmillan Publishing Co., 1980. 489]**PEER REVIEWED**

SIX SUBJECTS EXPOSED TO **TOLUENE** IN INSPIRED AIR (50, 100, 150 PPM) SHOWED LITTLE DIFFERENCE IN RATE OF RESP SOLVENT UPTAKE. NO SIMPLE RELATION EXISTED BETWEEN UPTAKE RATE & PERIPHERAL VENOUS CONCN, INDICATING THAT NO CALCULATION COULD BE MADE FOR TOXIC DOSE OF INNER ORGANS. DIFFERENCES IN RESP EXCRETION WAS EXPLAINED BY RESP MINUTE VOL IN POST-EXPOSURE PERIOD, &, AFTER EXPOSURE AT REST, THE AMT OF BODY FAT.
[VEULEMAN H ET AL; INT ARCH OCCUP ENVIRON HEALTH 42 (2): 105 (1978)]**PEER REVIEWED**

FOLLOWING SINGLE IP ADMIN OF (14)C-LABELED **TOLUENE** (290 UG/KG) TO MICE, HIGHEST LEVEL OF RADIOACTIVITY WAS FOUND IN ADIPOSE TISSUE, FOLLOWED IN DESCENDING ORDER BY KIDNEY, LIVER & LUNG. LOWEST ACTIVITY WAS IN BRAIN TISSUE & BLOOD/BRAIN RATIO WAS ABOUT 0.4.
[KOGA K; FOLIA PHARMACOL JPN 74 (6): 687 (1978)]**PEER REVIEWED**

The blood/gas partition coefficient ranges from 12.4 to 15.6.
[NRC; Alkyl Benzenes p.220 (1981)]**PEER REVIEWED**

At equilibrium, the avg **toluene** concn per liter of blood is 2.4 mg for each 100 ppm **toluene** in the envir air.
[Cleland, J.G., G.L. Kingsbury. Multimedia Environmental Goals for Environmental Assessment. Volume 1. EPA-600/7-77-136a. Research Triangle Park, NC: EPA, Nov. 1977.,p. E-146]**PEER REVIEWED**

... Whole body autoradiography has been modified and applied to distribution studies of ... **toluene**. ...
[Bergman K; CRC Crit Review Toxicol 12 (1): 59-118 (1983)]**PEER REVIEWED**

The urinary excretion of hippuric acid and o-cresol in humans was measured after a 7 hr exposure to

toluene at a constant concn of 100 ppm but with a time-weighted avg of 100 ppm. In study A, 4 men were exposed to clean air and to constant and varying concns of **toluene** in combination with rest and with 100 W exercise for 140 min exercise increased the end-exposure excretion rate of hippuric acid and o-cresol by 47 and 114%, respectively. After exposure, all excess hippuric acid was excreted within 4 hr, while o-cresol was eliminated with a half-life of approx 3 hr. Alveolar air concn of **toluene** was 21-31 ppm during constant exposure and 13-57 ppm during varying exposure, but no difference in mean alveolar **toluene** concn or in metabolite excretion was seen between the exposure schedules. In study B, 32 men and 39 women aged between 31 and 50 yr were exposed once to either clean air or ... or varying concns of **toluene**. The background excretion rate of hippuric acid was 0.97 mg/min (1.25 g/g creatinine) and rose to 3.74 mg/min (3.90 g/g creatinine) during the last 3 hr of exposure to 100 pmm **toluene**. The corresponding figures for o-cresol were 0.05 ug/min (0.08 mg/g creatinine), and 2.04 ug/min (2.05 mg/g creatinine). The individual creatinine excretion rate was considerably influenced by sex, body wt, and smoking habits, thus influencing the metabolite concn standardized in relation to creatinine. Thus, both metabolites are estimates of **toluene** exposure; o-cresol is more specific than hippuric acid, but the individual variation in excretion of both metabolites is large, and when implementing either of them as biological exposure indexes, the influence of sex, body size, age as well as consumption of tobacco and alcohol has to be considered.
[Baelum J et al; Int Arch Occup Environ Health 59 (3): 281-94 (1987)]**PEER REVIEWED**

The distribution of radioactivity in pregnant mice was registered at different time intervals (0-24 hr) after a 10 min period of inhalation of **toluene**. ... Autoradiographic and liq scintillation methods were used to make possible the distinction between volatile, water sol, and firmly tissue bound radioactivity. **Toluene** reached high concns immediately after inhalation in lipid rich tissues (brain and fat) and well perfused organs (liver and kidney) but were rapidly eliminated resulting in low concns at 1 hr in all maternal tissues, except fat. Metabolites reached peak levels around 30 min to 1 hr after inhalation, but were also relatively rapidly eliminated. ... One exception was the very strong accumulation of water sol metabolites at 4 and 24 hr in the nasal mucosa and olfactory bulb after inhalation of **toluene**. Volatile radioactivity was observed in the placenta and fetuses immediately and up to 1 hr after inhalation of solvent at all stages of gestation. The fetal levels were, however, much lower than in maternal tissues. In early gestation, an even distribution pattern was observed, while the fetal liver reached a higher concn than other fetal tissues in late gestation. In similarity with maternal tissues, fetal tissues reached the highest levels of metabolites 30 min to 1 hr after inhalation. A retention in uterine fluid was seen at 4 hr. Otherwise no retention of metabolites was observed in the fetoplacental unit. No firmly tissue bound metabolites of the studied solvents were observed in the fetal tissues in late gestation, indicating no fetal capacity for formation of reactive metabolites.
[Ghantous H, Danielson BRG; Biol Res Pregnancy Perinatol 7 (3): 98-105 (1986)]**PEER REVIEWED**

A study was instituted to determine whether gavage dosing and inhalation exposure resulted in similar blood levels of **toluene**. Groups of male Sprague-Dawley rats were dosed with **toluene** either by gavage with 0.10, 0.25, 0.50, or 1.0 mg/kg/body weight or through exposure to atmospheres containing 200 to 1000 ppm **toluene**. Blood samples were taken at 0.5, 1.0, 2.0, 4.0, 6.0, and 24.0 hours following dosing. Steady state blood concentrations were reached for both inhaled doses within 30 minutes of the exposure. After 6 hours the steady state **toluene** blood concentrations for the 200 and 1000 ppm dose levels were 2.89 and 37.23 ppm, respectively. For the oral doses, the peak blood **toluene** concentration increased

with increasing dosage. Blood profiles from higher oral doses more closely approximated the steady state inhalation blood profiles. At 24 hours following dosing, blood **toluene** levels from all doses by either route were below detectable levels, suggesting minimal carry over of **toluene** concentrations from one day to the next. An equation was derived which will allow the gavage dose of **toluene** to be made equivalent to an inhalation dose. Based on results of other studies, it was suggested that blood **toluene** levels following sc injection more closely resemble those obtained following inhalation than do blood levels after gavage. However, it is possible to obtain blood concentrations of **toluene** similar to those generated by a 6 hour inhalation exposure to 1000 ppm through gavage dosing.
[Sullivan MJ, Conolly RB; Environ Research 45 (1): 64-70 (1988)]**PEER REVIEWED**

An investigation was carried out to quantitate the effect of pulmonary ventilation on uptake and biological concentrations of six organic solvents. Tested solvents were acetone, styrene, **toluene**, xylenes, methylchloroform, and tetrachloroethylene. Lung uptake and urinary concentration (Cu) were measured in 15 volunteers, 24 to 52 years old, exposed in a chamber for 2 or 4 hours at rest, 2 hours with three alternations of light exercise, 1 hour of light exercise, or 30 minutes or more strenuous exercise. Environmental levels and urinary concentration were measured in 528 occupationally exposed workers before and after 4 hours of work at a light task (pulmonary ventilation 12 to 18 liters per minute). For volunteers, uptake and urinary concentration values were significantly correlated. Environmental levels and urinary concentration showed a close relationship for occupational exposure. Biological equivalent exposure limits corresponding to threshold limit value (TLV) time weighted averages were derived from urinary concentration values. For acetone, styrene, and xylenes, uptake for a given time and exposure level was dependent only on ventilation. The **toluene** retention index was slightly lower for exercise than for rest, and uptake was ventilation dependent during rest and ventilation and retention index dependent during exercise. Retention indices decreased with increasing ventilation at rest and during exercise for tetrachloroethylene and methylchloroform. Their urinary concentration values were ventilation and retention index dependent. Methylchloroform uptake was higher during light versus heavy exercise. It was concluded that work load profoundly affects the absorbed amount of chemical and should be a factor in implementation of biological exposure indices and TLVs.
[Pezzagno G et al; Am Ind Hygiene Assoc J 49 (11): 546-52 (1988)]**PEER REVIEWED**

Animal studies indicate that **toluene** readily crosses the placenta.
[Ellenhorn, M.J., S. Schonwald, G. Ordog, J. Wasserberger. Ellenhorn's Medical Toxicology: Diagnosis and Treatment of Human Poisoning. 2nd ed. Baltimore, MD: Williams and Wilkins, 1997. 166]**PEER REVIEWED**

When dogs were exposed to 0.4-0.6 ug/ml **toluene** vapor, 91-94% was taken up in the lungs. Absorption was complete when **toluene** was given orally to dogs; the blood level in rats increased more slowly after oral administration than after inhalation. Absorption through the skin of mice in vivo was 4.50 ug/sq cm per hour. **Toluene** penetrated rat skin excised three days after clipping and depilation with cream at a rate one-tenth that of benzene and ten times that of ortho-xylene.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47 93 (1989)]**PEER REVIEWED**

Toluene levels in brain and blood were linearly related to **toluene** levels in inhaled air after rats were exposed to 50, 100, 500, or 1000 ppm (189, 377, 1885, or 3770 mg/cu m) **toluene** for 3 hr.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47 93 (1989)]**PEER REVIEWED**

When rabbits were given a single oral dose of 350 mg/kg bw **toluene**, 19% was exhaled unchanged within 12 hr.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47 94 91989)]**PEER REVIEWED**

Pregnant C57B1 mice were exposed by inhalation to 14C-**toluene** (theoretical concentration, 2000 ppm (7540 mg/cu m)) for 10 min on days 11, 14 or 17 of gestation, and distribution of the label was determined 0, 0.5, 1, 4 and 24 hr after exposure. The label quickly entered the embryo, but uptake was low relative to that in maternal tissues. All fetal activity was extractable, indicating that no firmly bound metabolite was present.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47 94 (1989)]**PEER REVIEWED**

In humans, up to 75% of inhaled **toluene** is metabolized to hippuric acid and excreted in the urine within 12 hr of exposure. The remainder of the **toluene** is mainly excreted unchanged with a small percent being excreted as a sulfate or glucuronide of cresol.
[Sullivan, J.B. Jr., G.R. Krieger (eds.). Hazardous Materials Toxicology-Clinical Principles of Environmental Health. Baltimore, MD: Williams and Wilkins, 1992. 1091]**PEER REVIEWED**

The uptake of **toluene** in the blood is doubled during physical activity compared to the uptake at rest.
[Zenz, C., O.B. Dickerson, E.P. Horvath. Occupational Medicine. 3rd ed. St. Louis, MO., 1994 723]**PEER REVIEWED**

In nude mice exposure to 300, 1000, or 3000 ppm **toluene** under conditions where there was no respiratory intake of **toluene**, led to a dose-related and duration-related increase in whole body **toluene** levels. The calculated skin absorption coefficient was 1.24 cm/hr. The skin absorption rate for the 300 ppm concentration was 0.0009 mg/sq cm/hr; for the 1000 ppm concentration , it was 0.0046 mg/sq cm/hr; and for the 3000 ppm concentration, it was 0.0144 mg/sq cm/hr.
[Tsuruta H; Ind Health 27: 37-47 (1989) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.68 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

In humans, the **toluene** is distributed between the plasma and red blood cells at approximately a 1:1 ratio according to in vitro data; in rats, the ratio is 1:2 based on in vivo data.
[Lam CW et al; Toxicol Appl Pharmacol 104: 117-29 (1990) as cited in

U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.68 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

In one human who died 30 min after ingestion of 625 mg/kg **toluene**, the liver was found to have the highest concentration of **toluene** (133.5 ug/g) followed by the pancreas (88.2 ug/g), brain (85.3 ug/g), heart (62.6 ug/g), blood (12.2 ug/g), body fat (12.2 ug/g), and cerebrospinal fluid (11.1 ug/g).
[Ameno K et al; Forensic Sci Int 41: 255-60 (1989) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.71 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

Biological Half-Life:

0.083 days (Inhaled as environmental air)
[Cleland, J.G., G.L. Kingsbury. Multimedia Environmental Goals for Environmental Assessment. Volume 1. EPA-600/7-77-136a. Research Triangle Park, NC: EPA, Nov. 1977.,p. E-146]**PEER REVIEWED**

Mechanism of Action:

... **Toluene** at low concn /less than 100 ppm/ may produce disturbances in dopaminergic mechanisms of the basal ganglia probably leading to functional changes in sensory-motor integration. ...
[Fuxe K et al; Toxicol Lett 12 (2-3): 115-23 (1982)]**PEER REVIEWED**

Exposure to **toluene** causes both reversible and irreversible changes in the central nervous system. The effects of **toluene** inhalation on some specific enzymes and glutamate and GABA receptor binding in defined parts of the rat brain were studied following several exposure schemes. The activities of the transmitter synthesizing enzymes glutamic acid decarboxylase (GAD), choline acetyltransferase (ChAT) and aromatic amino-acid decarboxylase (AAD) were used as markers for permanent loss of neuronal activity. Catecholaminergic neurons showed a 50% reduction in the brain stem after 4 weeks exposure to 250 and 1000 ppm **toluene**. Following 500 ppm of **toluene**, 16 hr/day for 3 months, a general increase in the activities was seen. This is most probably due to a reduction in total protein content, to which the activities were related. The neurotransmitters glutamate and GABA had their specific receptor binding increased in most of the brain areas studied, but decreased in some areas. The glial enzyme, glutamine synthetase, has its activity increased in the cerebellar hemisphere following 4 weeks exposure to 1000 ppm. This suggests that glial cells in the area may have proliferated, a frequent phenomenon following CNS damage.
[Bjornaes S, Naalsund Lu; Toxicol 49 (2-3): 367-74 (1988)]**PEER REVIEWED**

The effect of styrene, **toluene**, ethylbenzene, alpha-methylstyrene, and butylbenzene on oxidative phosphorylation was studied using rat liver mitochondrial preparations. Rat liver mitochondria were prepared from male white Wistar rats and assessed for respiration rate, oxygen uptake, glutamate oxidation, succinate oxidation, ATPase activity, and proton permeability in the presence and absence of the alkyl benzene derivatives. Inclusion of the alkyl benzene derivatives in the incubation medium produced an initial acceleration of oxygen consumption followed by an inhibition of glutamate oxidation, and the stimulatory effect paralleled the aliphatic chain length. Glutamate oxidation was also inhibited by

styrene, ethylbenzene, and alpha-methylstyrene but not by butylbenzene or **toluene** in 2,4-dinitrophenol uncoupled mitochondria. Styrene and the aliphatic benzene derivative stimulated succinate oxidation in rat liver mitochondria without effect on 2,4-dinitrophenol stimulated succinate oxidation. Similar stimulatory effects on ATPase activity were observed with maximal stimulation occurring at the same relative concentrations producing maximal succinate oxidation. ATPase stimulation required magnesium, was oligomycin sensitive, and showed an inverse relation to the hydrophobicity of the compounds tested. The inclusion of styrene in the incubation medium markedly increased the rate of passive entry of protons into rat liver mitochondria in a manner comparable to 2,4-dinitrophenol. It was concluded that styrene and other monosubstituted benzene derivatives act as mitochondrial uncoupling agents.
[Mickiewicz W, Rzeczycki W; Biochem Pharmacol 37 (23): 4439-44 (1988)]**PEER REVIEWED**

Interactions:

IP LD50 OF **TOLUENE** FOR MALE MICE WAS 1.15 G/KG. PRETREATMENT WITH PHENOBARBITAL, PRODUCED MARKED DECR IN SLEEP INDUCED BY TEST DOSE (0.96 G/KG IP) OF **TOLUENE**. PRETREATMENT WITH HEPATIC ENZYME INHIBITORS SUCH AS CARBON TETRACHLORIDE, 2-DIETHYLAMINOETHYL-2,2-DIPHENYLATE HYDROCHLORIDE, PYRAZOLE & CYANAMIDE PRODUCED INCR IN SLEEP & DEATH ASSOC WITH PROLONGATION OF SLEEPING TIME.
[KOGA K, OHMIYA Y; J TOXICOL SCI 3 (1): 25 (1978)]**PEER REVIEWED**

TOLUENE WITH ASPHALT FUMES OR CHLORINATED HYDROCARBONS, SUCH AS TRICHLOROETHYLENE & TETRACHLOROETHENE, CAUSES DEPRESSION OF HYDROXYLATION & URINARY CONJUGATE EXCRETIONS. ... COMBINED EXPOSURE TO **TOLUENE**, XYLENE, FORMALDEHYDE, & ANILINE DYES DECR GRANULOCYTIC PHOSPHATASE ACTIVITY. CONVERSELY, HYDROGEN PEROXIDE ADMIN TO RATS INCR THE BLOOD PEROXIDE ACTIVITY & INCR THE TOLERANCE TO **TOLUENE**, AS DID PHENOBARBITAL IN SPECIFIC QUANTITIES.
[Clayton, G. D. and F. E. Clayton (eds.). Patty's Industrial Hygiene and Toxicology: Volume 2A, 2B, 2C: Toxicology. 3rd ed. New York: John Wiley Sons, 1981-1982. 3289]**PEER REVIEWED**

SPRAGUE-DAWLEY RATS WERE EXPOSED BY INHALATION TO **TOLUENE** (500, 1500, & 3000 PPM) FOR 3 DAYS. **TOLUENE** INCR CONCN OF LIVER MICROSOMAL CYTOCHROME P-450. A DOSE-DEPENDENT INCR IN THE IN VITRO LIVER MICROSOMAL FORMATION OF SEVERAL METABOLITES OF BIPHENYL & BENZO(A)PYRENE WAS OBSERVED FOR **TOLUENE**. **TOLUENE** MODIFIED THE METABOLISM AND TOXICITY OF OTHER ENVIRONMENTAL CONTAMINANTS.
[TOFTGARD R ET AL; ACTA PHARMACOL TOXICOL 51 (2): 108 (1982)]**PEER REVIEWED**

Perchloroethylene enhances toxicity of **toluene** admin orally in rats.
[USEPA; Health Assessment Document: Toluene p.15-1 (1982) EPA-800/8-82-008]**PEER REVIEWED**

Toluene and trichloroethylene seem to exhibit competitive inhibition.
[Ikeda M; Int Arch Arbeitsmed 33 (2): 125 (1974)]**PEER REVIEWED**

CFY rats ... on day 12 of pregnancy ... dams were given: 0, 125, 250, 500 and 3,600 mg/cu m ... and 250 mg/kg acetylsalicylic acid by gavage; two subgroups ... treated with 250 mg/kg acetylsalicylic acid in combination with 3,600 mg/cu m **toluene** inhalation were given 0, 2.5, or 5 gm/kg glycine 2 hours before the acetylsalicylic acid dose. ... **Toluene** was found to potentiate the toxic effect of acetylsalicylic acid and to increase both maternal and embryonic toxicity ... increasing acetylsalicylic acid embryotoxicity caused by **toluene** can be warded off by glycine administration.
[Ungvary G et al; Teratology 27 (2): 261-9 (1983)]**PEER REVIEWED**

The metabolic interaction of **toluene** and ethanol was studied in male rabbits having received ethanol (26.0 mmol/kg po), **toluene** (5.4 mmol/kg po) or both. Compared with ethanol alone, **toluene** given 2 hr after ethanol caused a significantly higher and more prolonged concentration of blood alcohol. A similar trend of blood alcohol was observed at the later stage with **toluene** given prior to ethanol. On the other hand, with simultaneous doses of the two substances, the blood **toluene** concentration was higher for the first 15-30 min than the ethanol control and the urinary excretion of hippuric acid, a main metabolite of **toluene**, was markedly decreased for the first 2 hr. The blood ethanol in this group, on the contrary, was reduced until 1 hr after administration. These results indicate that **toluene** and ethanol act reciprocally as competitive inhibitors in their metabolism after single administrations.
[Takahashi S et al; Arch Toxicol 59 (5): 307-10 (1987)]**PEER REVIEWED**

In an experimental human study, the effect of **toluene** and ethanol (alone or in combination) on psychophysiologic functions was studied in 12 men (22-44 yr of age). Each subject served as his own control. Subjects were exposed to **toluene** by inhalation at a concentration of 300 mg **toluene**/cu m air for 4.5 hr. Ethanol was ingested at a dose equivalent to 15 mmol ethanol/kg body weight. **Toluene** had no significant effect on the 4 performance tests. A significant but weak depression of heart rate was observed during sleep latency tests (1-2.5 beats/min, $0.001 < p < 0.01$). There was a significant increase in reporting of headache ($p < 0.05$) and in reporting for all symptoms (nausea, headache, irritation) combined ($p < 0.05$). No interaction between ethanol and **toluene** was observed.
[Iregren A et al; Scand J Work Environ Health 12: 128-36 (1986)]**PEER REVIEWED**

Male Sprague-Dawley rats were used to study the renal toxicity potential of subchronic exposure to non-toxic doses of a combination of styrene and **toluene**. Four groups (n= 6) of rats were injected ip with: (1) 4 mmol styrene 2 times/day at 4 hr intervals; (2) 10 mmol **toluene**/kg once a day; (3) 4 mmol styrene/kg 2 times/day plus 10 mmol **toluene**/kg once/day; (4) All treatments were given 5 days/wk for 4 consecutive wk. By the fourth wk, there was a significant increase ($p < 0.05$) in urinary excretion of gamma-glutamyl transpeptidase, protein, and glucose by the group receiving combined treatment versus those receiving treatment with either chemical alone. There was an increase in excretion of hippuric acid in the mixture treatment group, but no increase in mandelic and phenylglyoxylic acids or thioethers. Blood urinary nitrogen was not modified by the individual chemicals or the mixture. Electron microscopic examination of the kidney showed an increase of single membrane vacuoles in the proximal convoluted tubules of rats treated with a mixture of chemicals, but not with **toluene** or styrene alone.
[Chakrabarti S, Tuchweber B; Toxicol Lett 39 (1): 27-34 (1987)]**PEER REVIEWED**

... **Toluene** has been shown to be a competitive inhibitor of the metabolism of benzene. This competitive interaction alleviates the metabolite-mediated toxicity of benzene ...

[Klaassen, C.D., M.O. Amdur, Doull J. (eds.). Casarett and Doull's Toxicology. The Basic Science of Poisons. 5th ed. New York, NY: McGraw-Hill, 1995. 741]**PEER REVIEWED**

Xenobiotic competitors for the same metabolic route, such as benzene and xylene, would ... have an impact on **toluene** metabolism.
[U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.95 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

... A single alcoholic drink has a very strong, acute inhibitory effect on the hepatic elimination of **toluene**.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V71 842 (1999)]**PEER REVIEWED**

The aim of this study was to examine if the drug chlorzoxazone has any influence on the toxicokinetics of acetone and **toluene**. Chlorzoxazone is mainly metabolized by the same enzyme (Cytochrome P450 2E1) as ethanol and many other organic solvents. Ten male volunteers were exposed to solvent vapor (2 hr, 50 watt) in an exposure chamber. Each subject was exposed to acetone only (250 ppm), acetone + chlorzoxazone, **toluene** (50 ppm) only, **toluene** + chlorzoxazone, and chlorzoxazone only. Chlorzoxazone (500 mg) was taken as two tablets 1 h prior to solvent exposure. Samples of blood, urine and exhaled air were collected before, during and until 20 h post exposure. The time-concentration curves of acetone and **toluene** in blood were fitted to one- and four-compartment toxicokinetic models, respectively. Except for a delayed excretion of hippuric acid in urine, no effects on the **toluene** toxicokinetics were seen after chlorzoxazone treatment. Small increases in chlorzoxazone plasma levels were seen after exposure compared to chlorzoxazone alone. These interactions, although statistically significant, seem to be small compared to the interindividual variability on metabolism and toxicokinetics.
[Ernstgard L et al; Toxicol Sci 48 (2): 189-96 (1999)]**PEER REVIEWED**

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Metabolism/Metabolites:

Toluene is extensively metabolized via oxidation to benzyl alcohol then to benzaldehyde by alcohol dehydrogenase. Further oxidation then forms benzoic acid. Conjugation with glycine produces the major metabolite, hippuric acid, which is excreted in the urine. Benzyl glucuronide is formed in smaller amounts by conjugation with glucuronic acid.
[Haddad, L.M., Clinical Management of Poisoning and Drug Overdose. 2nd ed. Philadelphia, PA: W.B. Saunders Co., 1990. 1224]**PEER REVIEWED**

IN PRINTERS EXPOSED TO AIR CONTAINING **TOLUENE** (AVG CONCN 23 PPM), URINARY EXCRETION OF O-CRESOL, WHICH IS NOT A NORMAL CONSTITUENT OF URINE, WAS OBSERVED. APPARENTLY, **TOLUENE** WAS OXIDIZED AT AROMATIC NUCLEUS FORMING CRESOLS, BESIDES HIPPURIC ACID.
[ANGERER J; INT ARCH OCCUP ENVIRON HEALTH 43 (1): 63 (1979)]**PEER REVIEWED**

In rats, approx 0.5%-1.1% of the dose is converted to o-cresol and p-cresol and is excreted as glucuronide and sulfate conjugates.
[Bakke OM, Scheline RR; Tox Appl Pharm 16: 691-700 (1970) as cited in NRC; Alkyl Benzenes p.221 (1981)]**PEER REVIEWED**

In mammalian species, acidic metabolites are conjugated with glycine to form hippuric acid and phenylacetic acid. In humans, the phenylacetic acid metabolite is also conjugated with glutamine to form phenacetylglutamine.
[James MO et al; Proc R Soc Lond Ser B 182: 25-35 (1972) as cited in NRC; Alkyl Benzenes p.219 (1981)]**PEER REVIEWED**

The association between occupational **toluene** exposure and blood and adipose tissue **toluene** concentrations was examined. Breathing zone samples were monitored for **toluene** in two Swedish rotogravure printing facilities. Sc adipose tissues were taken from 37 workers after work on Thursday or Friday and analyzed for **toluene**. Venous blood samples were taken from 11 workers after work on Friday and at various times over the following weekend and assayed for **toluene**. Blood and adipose tissue samples were obtained from 11 other workers immediately after work and after 63 and 135 hours nonexposure and analyzed for **toluene**. Blood samples were also taken from 21 unexposed workers and analyzed for **toluene**. Attempts were made to fit the blood **toluene** data to various pharmacokinetics models. Airborne **toluene** concentrations in the printing factories ranged from 8 to 416 mg/cu m, median 75 mg/cu m. Blood **toluene** concentrations in the unexposed workers were below the detection limit, 0.01 umole/l. Blood samples obtained immediately after work contained 0.22 to 21.4 umole/l **toluene**. Elimination of **toluene** from the blood could be described by a three compartment model having median halftimes of 9 minutes, 2 hours, and 79 hours. **Toluene** was eliminated from adipose tissue with a median halftime of 79 hours. Adipose tissue concentrations were significantly associated with the workers' exposure to airborne **toluene** during the previous week. Adipose tissue **toluene** concentrations were significantly correlated with blood **toluene** concentrations after 70 hours exposure. It was concluded that the prolonged presence of **toluene** in the blood means that there is an endogenous exposure from adipose

tissue depots that continues long after occupational exposure has ended.
[Nise G et al; Br J Ind Med 46 (6): 407-11 (1989)]**PEER REVIEWED**

Evidence has suggested that there is an ethnic related difference in organic solvent metabolism in humans; analyses were thus made to obtain evidence of strain differences in animals to assist in consolidating the observation in workers. Female Donryu, Fischer, Sprague-Dawley, and Wistar rats were exposed to **toluene** at dose levels of 5, 45, 500, 2500, and 3500 ppm for 8 hours in a dynamic flow type exposure system. Urine samples were collected for 24 hours from the start of exposure. While the variation in free p-cresol excretion was wide among the rats of the same strain exposed to **toluene** at the same concentration, it was also noted that the four strains tested could be classified into two groups depending on the free p-cresol levels at **toluene** concentrations up to 500 ppm. No significant differences were noted between Sprague-Dawley and Wistar strains nor between Donryu and Fischer strains at the 45 and 500 ppm levels. However, there were significant differences between these two groups. At higher concentrations of 2500 and 3500 ppm, the increase in the free p-cresol levels was remarkable only in Donryu rats, reaching the levels of Sprague-Dawley and Wistar rats, while the level in Fischer rats remained unchanged.
[Inoue O et al; Bull Environ Contam Toxicol 43 (1): 74-9 (1989)]**PEER REVIEWED**

The mutual metabolic suppression between benzene and **toluene** was studied. The subjects, 190 male Chinese workers employed in shoe manufacturing, printing, audio equipment manufacture, and automobile industries, were divided into four groups based on occupational exposure: 65 were exposed to benzene, 35 to **toluene**, 55 to both compounds, and 35 served as comparisons. The arithmetic mean exposure level of benzene was 31.9 and of **toluene** 44.7 ppm. The mixture contained benzene at 17.9 +/29.3 and **toluene** at 20.5 +/25.8 ppm. The exposure levels were measured using individuals diffusive samplers. The geometric mean levels of the metabolites, phenol, catechol, hydroquinone, hippuric acid, and o-cresol, in unexposed workers were 6.9, 9.4, 4.8, 72.5, and 0.066 mg per liter, respectively. Values corrected for creatinine and specific gravity were different from the values cited above. Multiple correlation coefficients for benzene exposure versus its three metabolites were for phenol, 0.740; for catechol, 0.629; and for hydroquinone, 0.726. Multiple correlation coefficients for **toluene** and its two metabolites were 0.649 for hippuric acid and 0.583 for o-cresol. The slopes of regression lines for the exposure to benzene in the presence of **toluene** were less than half of those obtained when the workers were exposed to benzene alone; however, the regression lines for benzene in mixture versus catechol were about 80% or higher than the lines observed with benzene as the sole pollutant. The regression lines for **toluene** in the mixture and excretion level of hippuric acid and o-cresol showed reduced metabolic conversion compared to when exposure was limited to **toluene** alone. It was concluded that simultaneous exposure to benzene and **toluene** results in mutual suppression of metabolism yielding the urinary metabolites phenol, hydroquinone, hippuric acid, and o-cresol.
[Inoue O et al; Int Arch Occup Environ Health 60 (1): 15-20 (1988)]**PEER REVIEWED**

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Absorption, Distribution & Excretion:

TOLUENE VAPOR IS READILY ABSORBED BY INHALATION AND THE LIQUID BY THE GI TRACT, BUT POORLY FROM THE SKIN.
[Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965. 68]**PEER REVIEWED**

IN DOGS SUBJECTED TO INHALATION ... HIGHEST CONCENTRATIONS WERE FOUND IN THE ADRENALS (20 UG/G), BRAIN (19 UG/G IN CEREBELLUM & 18 UG/G IN CEREBRUM), AND BONE MARROW (18 UG/G).
[Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965. 69]**PEER REVIEWED**

ALTHOUGH SOME ABSORBED **TOLUENE** MAY BE REEXHALED BY LUNG, MAJOR EXCRETORY PATHWAY IS RAPID OXIDATION OF **TOLUENE** TO BENZOIC ACID, WHICH IS CONJUGATED WITH GLYCINE & EXCRETED AS HIPPURIC ACID IN URINE. ... WITHIN REASONABLE LIMITS, EXCRETION OF HIPPURIC ACID IN URINE IS PROPORTIONAL TO EXPOSURE. AN EXPOSURE OF 200 PPM OF **TOLUENE** RESULTED IN EXCRETION OF 3.5 G HIPPURIC ACID PER LITER OF URINE (SPECIFIC GRAVITY 1.016).
[Doull, J., C.D. Klaassen, and M. D. Amdur (eds.). Casarett and Doull's Toxicology. 2nd ed. New York: Macmillan Publishing Co., 1980. 489]**PEER REVIEWED**

SIX SUBJECTS EXPOSED TO **TOLUENE** IN INSPIRED AIR (50, 100, 150 PPM) SHOWED LITTLE DIFFERENCE IN RATE OF RESP SOLVENT UPTAKE. NO SIMPLE RELATION EXISTED BETWEEN UPTAKE RATE & PERIPHERAL VENOUS CONCN, INDICATING THAT NO CALCULATION COULD BE MADE FOR TOXIC DOSE OF INNER ORGANS. DIFFERENCES IN RESP EXCRETION WAS EXPLAINED BY RESP MINUTE VOL IN POST-EXPOSURE PERIOD, &, AFTER EXPOSURE AT REST, THE AMT OF BODY FAT.
[VEULEMAN H ET AL; INT ARCH OCCUP ENVIRON HEALTH 42 (2): 105 (1978)]**PEER REVIEWED**

FOLLOWING SINGLE IP ADMIN OF (14)C-LABELED **TOLUENE** (290 UG/KG) TO MICE, HIGHEST LEVEL OF RADIOACTIVITY WAS FOUND IN ADIPOSE TISSUE, FOLLOWED IN DESCENDING ORDER BY KIDNEY, LIVER & LUNG. LOWEST ACTIVITY WAS IN BRAIN TISSUE & BLOOD/BRAIN RATIO WAS ABOUT 0.4.
[KOGA K; FOLIA PHARMACOL JPN 74 (6): 687 (1978)]**PEER REVIEWED**

The blood/gas partition coefficient ranges from 12.4 to 15.6.
[NRC; Alkyl Benzenes p.220 (1981)]**PEER REVIEWED**

At equilibrium, the avg **toluene** concn per liter of blood is 2.4 mg for each 100 ppm **toluene** in the envir air.
[Cleland, J.G., G.L. Kingsbury. Multimedia Environmental Goals for

Environmental Assessment. Volume 1. EPA-600/7-77-136a. Research Triangle Park, NC: EPA, Nov. 1977.,p. E-146]**PEER REVIEWED**

... Whole body autoradiography has been modified and applied to distribution studies of ... **toluene**. ... [Bergman K; CRC Crit Review Toxicol 12 (1): 59-118 (1983)]**PEER REVIEWED**

The urinary excretion of hippuric acid and o-cresol in humans was measured after a 7 hr exposure to **toluene** at a constant concn of 100 ppm but with a time-weighted avg of 100 ppm. In study A, 4 men were exposed to clean air and to constant and varying concns of **toluene** in combination with rest and with 100 W exercise for 140 min exercise increased the end-exposure excretion rate of hippuric acid and o-cresol by 47 and 114%, respectively. After exposure, all excess hippuric acid was excreted within 4 hr, while o-cresol was eliminated with a half-life of approx 3 hr. Alveolar air concn of **toluene** was 21-31 ppm during constant exposure and 13-57 ppm during varying exposure, but no difference in mean alveolar **toluene** concn or in metabolite excretion was seen between the exposure schedules. In study B, 32 men and 39 women aged between 31 and 50 yr were exposed once to either clean air or ... or varying concns of **toluene**. The background excretion rate of hippuric acid was 0.97 mg/min (1.25 g/g creatinine) and rose to 3.74 mg/min (3.90 g/g creatinine) during the last 3 hr of exposure to 100 pmm **toluene**. The corresponding figures for o-cresol were 0.05 ug/min (0.08 mg/g creatinine), and 2.04 ug/min (2.05 mg/g creatinine). The individual creatinine excretion rate was considerably influenced by sex, body wt, and smoking habits, thus influencing the metabolite concn standardized in relation to creatinine. Thus, both metabolites are estimates of **toluene** exposure; o-cresol is more specific than hippuric acid, but the individual variation in excretion of both metabolites is large, and when implementing either of them as biological exposure indexes, the influence of sex, body size, age as well as consumption of tobacco and alcohol has to be considered.
[Baelum J et al; Int Arch Occup Environ Health 59 (3): 281-94 (1987)]**PEER REVIEWED**

The distribution of radioactivity in pregnant mice was registered at different time intervals (0-24 hr) after a 10 min period of inhalation of **toluene**. ... Autoradiographic and liq scintillation methods were used to make possible the distinction between volatile, water sol, and firmly tissue bound radioactivity. **Toluene** reached high concns immediately after inhalation in lipid rich tissues (brain and fat) and well perfused organs (liver and kidney) but were rapidly eliminated resulting in low concns at 1 hr in all maternal tissues, except fat. Metabolites reached peak levels around 30 min to 1 hr after inhalation, but were also relatively rapidly eliminated. ... One exception was the very strong accumulation of water sol metabolites at 4 and 24 hr in the nasal mucosa and olfactory bulb after inhalation of **toluene**. Volatile radioactivity was observed in the placenta and fetuses immediately and up to 1 hr after inhalation of solvent at all stages of gestation. The fetal levels were, however, much lower than in maternal tissues. In early gestation, an even distribution pattern was observed, while the fetal liver reached a higher concn than other fetal tissues in late gestation. In similarity with maternal tissues, fetal tissues reached the highest levels of metabolites 30 min to 1 hr after inhalation. A retention in uterine fluid was seen at 4 hr. Otherwise no retention of metabolites was observed in the fetoplacental unit. No firmly tissue bound metabolites of the studied solvents were observed in the fetal tissues in late gestation, indicating no fetal capacity for formation of reactive metabolites.
[Ghantous H, Danielson BRG; Biol Res Pregnancy Perinatol 7 (3): 98-105 (1986)]**PEER REVIEWED**

A study was instituted to determine whether gavage dosing and inhalation exposure resulted in similar blood levels of **toluene**. Groups of male Sprague-Dawley rats were dosed with **toluene** either by gavage with 0.10, 0.25, 0.50, or 1.0 mg/kg/body weight or through exposure to atmospheres containing 200 to 1000 ppm **toluene**. Blood samples were taken at 0.5, 1.0, 2.0, 4.0, 6.0, and 24.0 hours following dosing. Steady state blood concentrations were reached for both inhaled doses within 30 minutes of the exposure. After 6 hours the steady state **toluene** blood concentrations for the 200 and 1000 ppm dose levels were 2.89 and 37.23 ppm, respectively. For the oral doses, the peak blood **toluene** concentration increased with increasing dosage. Blood profiles from higher oral doses more closely approximated the steady state inhalation blood profiles. At 24 hours following dosing, blood **toluene** levels from all doses by either route were below detectable levels, suggesting minimal carry over of **toluene** concentrations from one day to the next. An equation was derived which will allow the gavage dose of **toluene** to be made equivalent to an inhalation dose. Based on results of other studies, it was suggested that blood **toluene** levels following sc injection more closely resemble those obtained following inhalation than do blood levels after gavage. However, it is possible to obtain blood concentrations of **toluene** similar to those generated by a 6 hour inhalation exposure to 1000 ppm through gavage dosing.
[Sullivan MJ, Conolly RB; Environ Research 45 (1): 64-70 (1988)]**PEER REVIEWED**

An investigation was carried out to quantitate the effect of pulmonary ventilation on uptake and biological concentrations of six organic solvents. Tested solvents were acetone, styrene, **toluene**, xylenes, methylchloroform, and tetrachloroethylene. Lung uptake and urinary concentration (Cu) were measured in 15 volunteers, 24 to 52 years old, exposed in a chamber for 2 or 4 hours at rest, 2 hours with three alternations of light exercise, 1 hour of light exercise, or 30 minutes or more strenuous exercise. Environmental levels and urinary concentration were measured in 528 occupationally exposed workers before and after 4 hours of work at a light task (pulmonary ventilation 12 to 18 liters per minute). For volunteers, uptake and urinary concentration values were significantly correlated. Environmental levels and urinary concentration showed a close relationship for occupational exposure. Biological equivalent exposure limits corresponding to threshold limit value (TLV) time weighted averages were derived from urinary concentration values. For acetone, styrene, and xylenes, uptake for a given time and exposure level was dependent only on ventilation. The **toluene** retention index was slightly lower for exercise than for rest, and uptake was ventilation dependent during rest and ventilation and retention index dependent during exercise. Retention indices decreased with increasing ventilation at rest and during exercise for tetrachloroethylene and methylchloroform. Their urinary concentration values were ventilation and retention index dependent. Methylchloroform uptake was higher during light versus heavy exercise. It was concluded that work load profoundly affects the absorbed amount of chemical and should be a factor in implementation of biological exposure indices and TLVs.
[Pezzagno G et al; Am Ind Hygiene Assoc J 49 (11): 546-52 (1988)]**PEER REVIEWED**

Animal studies indicate that **toluene** readily crosses the placenta.
[Ellenhorn, M.J., S. Schonwald, G. Ordog, J. Wasserberger. Ellenhorn's Medical Toxicology: Diagnosis and Treatment of Human Poisoning. 2nd ed. Baltimore, MD: Williams and Wilkins, 1997. 166]**PEER REVIEWED**

When dogs were exposed to 0.4-0.6 ug/ml **toluene** vapor, 91-94% was taken up in the lungs. Absorption was complete when **toluene** was given orally to dogs; the blood level in rats increased more slowly after oral administration than after inhalation. Absorption through the skin of mice in vivo was 4.50 ug/sq cm

per hour. **Toluene** penetrated rat skin excised three days after clipping and depilation with cream at a rate one-tenth that of benzene and ten times that of ortho-xylene.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47 93 (1989)]**PEER REVIEWED**

Toluene levels in brain and blood were linearly related to **toluene** levels in inhaled air after rats were exposed to 50, 100, 500, or 1000 ppm (189, 377, 1885, or 3770 mg/cu m) **toluene** for 3 hr.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47 93 (1989)]**PEER REVIEWED**

When rabbits were given a single oral dose of 350 mg/kg bw **toluene**, 19% was exhaled unchanged within 12 hr.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47 94 91989)]**PEER REVIEWED**

Pregnant C57B1 mice were exposed by inhalation to 14C-**toluene** (theoretical concentration, 2000 ppm (7540 mg/cu m)) for 10 min on days 11, 14 or 17 of gestation, and distribution of the label was determined 0, 0.5, 1, 4 and 24 hr after exposure. The label quickly entered the embryo, but uptake was low relative to that in maternal tissues. All fetal activity was extractable, indicating that no firmly bound metabolite was present.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47 94 (1989)]**PEER REVIEWED**

In humans, up to 75% of inhaled **toluene** is metabolized to hippuric acid and excreted in the urine within 12 hr of exposure. The remainder of the **toluene** is mainly excreted unchanged with a small percent being excreted as a sulfate or glucuronide of cresol.
[Sullivan, J.B. Jr., G.R. Krieger (eds.). Hazardous Materials Toxicology-Clinical Principles of Environmental Health. Baltimore, MD: Williams and Wilkins, 1992. 1091]**PEER REVIEWED**

The uptake of **toluene** in the blood is doubled during physical activity compared to the uptake at rest.
[Zenz, C., O.B. Dickerson, E.P. Horvath. Occupational Medicine. 3rd ed. St. Louis, MO., 1994 723]**PEER REVIEWED**

In nude mice exposure to 300, 1000, or 3000 ppm **toluene** under conditions where there was no respiratory intake of **toluene**, led to a dose-related and duration-related increase in whole body **toluene** levels. The calculated skin absorption coefficient was 1.24 cm/hr. The skin absorption rate for the 300 ppm concentration was 0.0009 mg/sq cm/hr; for the 1000 ppm concentration , it was 0.0046 mg/sq cm/hr; and for the 3000 ppm concentration, it was 0.0144 mg/sq cm/hr.
[Tsuruta H; Ind Health 27: 37-47 (1989) as cited in U.S. Dept Health &

Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.68 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

In humans, the **toluene** is distributed between the plasma and red blood cells at approximately a 1:1 ratio according to in vitro data; in rats, the ratio is 1:2 based on in vivo data.
[Lam CW et al; Toxicol Appl Pharmacol 104: 117-29 (1990) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.68 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

In one human who died 30 min after ingestion of 625 mg/kg **toluene**, the liver was found to have the highest concentration of **toluene** (133.5 ug/g) followed by the pancreas (88.2 ug/g), brain (85.3 ug/g), heart (62.6 ug/g), blood (12.2 ug/g), body fat (12.2 ug/g), and cerebrospinal fluid (11.1 ug/g).
[Ameno K et al; Forensic Sci Int 41: 255-60 (1989) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.71 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

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Biological Half-Life:

0.083 days (Inhaled as environmental air)
[Cleland, J.G., G.L. Kingsbury. Multimedia Environmental Goals for Environmental Assessment. Volume 1. EPA-600/7-77-136a. Research Triangle Park, NC: EPA, Nov. 1977.,p. E-146]**PEER REVIEWED**

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Mechanism of Action:

... **Toluene** at low concn /less than 100 ppm/ may produce disturbances in dopaminergic mechanisms of the basal ganglia probably leading to functional changes in sensory-motor integration. ...
[Fuxe K et al; Toxicol Lett 12 (2-3): 115-23 (1982)]**PEER REVIEWED**

Exposure to **toluene** causes both reversible and irreversible changes in the central nervous system. The effects of **toluene** inhalation on some specific enzymes and glutamate and GABA receptor binding in defined parts of the rat brain were studied following several exposure schemes. The activities of the transmitter synthesizing enzymes glutamic acid decarboxylase (GAD), choline acetyltransferase (ChAT) and aromatic amino-acid decarboxylase (AAD) were used as markers for permanent loss of neuronal activity. Catecholaminergic neurons showed a 50% reduction in the brain stem after 4 weeks exposure to 250 and 1000 ppm **toluene**. Following 500 ppm of **toluene**, 16 hr/day for 3 months, a general increase in the activities was seen. This is most probably due to a reduction in total protein content, to which the activities were related. The neurotransmitters glutamate and GABA had their specific receptor binding increased in most of the brain areas studied, but decreased in some areas. The glial enzyme, glutamine synthetase, has its activity increased in the cerebellar hemisphere following 4 weeks exposure to 1000 ppm. This suggests that glial cells in the area may have proliferated, a frequent phenomenon following CNS damage.
[Bjornaes S, Naalsund Lu; Toxicol 49 (2-3): 367-74 (1988)]**PEER REVIEWED**

The effect of styrene, **toluene**, ethylbenzene, alpha-methylstyrene, and butylbenzene on oxidative phosphorylation was studied using rat liver mitochondrial preparations. Rat liver mitochondria were prepared from male white Wistar rats and assessed for respiration rate, oxygen uptake, glutamate oxidation, succinate oxidation, ATPase activity, and proton permeability in the presence and absence of the alkyl benzene derivatives. Inclusion of the alkyl benzene derivatives in the incubation medium produced an initial acceleration of oxygen consumption followed by an inhibition of glutamate oxidation, and the stimulatory effect paralleled the aliphatic chain length. Glutamate oxidation was also inhibited by styrene, ethylbenzene, and alpha-methylstyrene but not by butylbenzene or **toluene** in 2,4-dinitrophenol uncoupled mitochondria. Styrene and the aliphatic benzene derivative stimulated succinate oxidation in rat liver mitochondria without effect on 2,4-dinitrophenol stimulated succinate oxidation. Similar stimulatory effects on ATPase activity were observed with maximal stimulation occurring at the same relative concentrations producing maximal succinate oxidation. ATPase stimulation required magnesium, was oligomycin sensitive, and showed an inverse relation to the hydrophobicity of the compounds tested. The inclusion of styrene in the incubation medium markedly increased the rate of passive entry of protons into rat liver mitochondria in a manner comparable to 2,4-dinitrophenol. It was concluded that styrene and other monosubstituted benzene derivatives act as mitochondrial uncoupling agents.
[Mickiewicz W, Rzeczycki W; Biochem Pharmacol 37 (23): 4439-44 (1988)]**PEER REVIEWED**

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Interactions:

IP LD50 OF **TOLUENE** FOR MALE MICE WAS 1.15 G/KG. PRETREATMENT WITH PHENOBARBITAL, PRODUCED MARKED DECR IN SLEEP INDUCED BY TEST DOSE (0.96 G/KG IP) OF **TOLUENE**. PRETREATMENT WITH HEPATIC ENZYME INHIBITORS SUCH AS CARBON TETRACHLORIDE, 2-DIETHYLAMINOETHYL-2,2-DIPHENYLATE HYDROCHLORIDE, PYRAZOLE & CYANAMIDE PRODUCED INCR IN SLEEP & DEATH ASSOC WITH PROLONGATION OF SLEEPING TIME.
[KOGA K, OHMIYA Y; J TOXICOL SCI 3 (1): 25 (1978)]**PEER REVIEWED**

TOLUENE WITH ASPHALT FUMES OR CHLORINATED HYDROCARBONS, SUCH AS TRICHLOROETHYLENE & TETRACHLOROETHENE, CAUSES DEPRESSION OF HYDROXYLATION & URINARY CONJUGATE EXCRETIONS. ... COMBINED EXPOSURE TO **TOLUENE**, XYLENE, FORMALDEHYDE, & ANILINE DYES DECR GRANULOCYTIC PHOSPHATASE ACTIVITY. CONVERSELY, HYDROGEN PEROXIDE ADMIN TO RATS INCR THE BLOOD PEROXIDE ACTIVITY & INCR THE TOLERANCE TO **TOLUENE**, AS DID PHENOBARBITAL IN SPECIFIC QUANTITIES.
[Clayton, G. D. and F. E. Clayton (eds.). Patty's Industrial Hygiene and Toxicology: Volume 2A, 2B, 2C: Toxicology. 3rd ed. New York: John Wiley Sons, 1981-1982. 3289]**PEER REVIEWED**

SPRAGUE-DAWLEY RATS WERE EXPOSED BY INHALATION TO **TOLUENE** (500, 1500, & 3000 PPM) FOR 3 DAYS. **TOLUENE** INCR CONCN OF LIVER MICROSOMAL CYTOCHROME P-450. A DOSE-DEPENDENT INCR IN THE IN VITRO LIVER MICROSOMAL FORMATION OF SEVERAL METABOLITES OF BIPHENYL & BENZO(A)PYRENE WAS OBSERVED FOR **TOLUENE**. **TOLUENE** MODIFIED THE METABOLISM AND TOXICITY OF OTHER ENVIRONMENTAL CONTAMINANTS.
[TOFTGARD R ET AL; ACTA PHARMACOL TOXICOL 51 (2): 108 (1982)]**PEER REVIEWED**

Perchloroethylene enhances toxicity of **toluene** admin orally in rats.
[USEPA; Health Assessment Document: Toluene p.15-1 (1982) EPA-800/8-82-008]**PEER REVIEWED**

Toluene and trichloroethylene seem to exhibit competitive inhibition.
[Ikeda M; Int Arch Arbeitsmed 33 (2): 125 (1974)]**PEER REVIEWED**

CFY rats ... on day 12 of pregnancy ... dams were given: 0, 125, 250, 500 and 3,600 mg/cu m ... and 250 mg/kg acetylsalicylic acid by gavage; two subgroups ... treated with 250 mg/kg acetylsalicylic acid in combination with 3,600 mg/cu m **toluene** inhalation were given 0, 2.5, or 5 gm/kg glycine 2 hours before the acetylsalicylic acid dose. ... **Toluene** was found to potentiate the toxic effect of acetylsalicylic acid and to increase both maternal and embryonic toxicity ... increasing acetylsalicylic acid embryotoxicity caused by **toluene** can be warded off by glycine administration.
[Ungvary G et al; Teratology 27 (2): 261-9 (1983)]**PEER REVIEWED**

The metabolic interaction of **toluene** and ethanol was studied in male rabbits having received ethanol (26.0 mmol/kg po), **toluene** (5.4 mmol/kg po) or both. Compared with ethanol alone, **toluene** given 2 hr after ethanol caused a significantly higher and more prolonged concentration of blood alcohol. A similar trend of blood alcohol was observed at the later stage with **toluene** given prior to ethanol. On the other hand, with simultaneous doses of the two substances, the blood **toluene** concentration was higher for the first 15-30 min than the ethanol control and the urinary excretion of hippuric acid, a main metabolite of **toluene**, was markedly decreased for the first 2 hr. The blood ethanol in this group, on the contrary, was reduced until 1 hr after administration. These results indicate that **toluene** and ethanol act reciprocally as competitive inhibitors in their metabolism after single administrations.
[Takahashi S et al; Arch Toxicol 59 (5): 307-10 (1987)]**PEER REVIEWED**

In an experimental human study, the effect of **toluene** and ethanol (alone or in combination) on psychophysiologic functions was studied in 12 men (22-44 yr of age). Each subject served as his own control. Subjects were exposed to **toluene** by inhalation at a concentration of 300 mg **toluene**/cu m air for 4.5 hr. Ethanol was ingested at a dose equivalent to 15 mmol ethanol/kg body weight. **Toluene** had no significant effect on the 4 performance tests. A significant but weak depression of heart rate was observed during sleep latency tests (1-2.5 beats/min, 0.001 <p< 0.01). There was a significant increase in reporting of headache (p< 0.05) and in reporting for all symptoms (nausea, headache, irritation) combined (p< 0.05). No interaction between ethanol and **toluene** was observed.
[Iregren A et al; Scand J Work Environ Health 12: 128-36 (1986)]**PEER REVIEWED**

Male Sprague-Dawley rats were used to study the renal toxicity potential of subchronic exposure to non-toxic doses of a combination of styrene and **toluene**. Four groups (n= 6) of rats were injected ip with: (1) 4 mmol styrene 2 times/day at 4 hr intervals; (2) 10 mmol **toluene**/kg once a day; (3) 4 mmol styrene/kg 2 times/day plus 10 mmol **toluene**/kg once/day; (4) All treatments were given 5 days/wk for 4 consecutive wk. By the fourth wk, there was a significant increase (p< 0.05) in urinary excretion of gamma-glutamyl transpeptidase, protein, and glucose by the group receiving combined treatment versus those receiving treatment with either chemical alone. There was an increase in excretion of hippuric acid in the mixture treatment group, but no increase in mandelic and phenylglyoxylic acids or thioethers. Blood urinary nitrogen was not modified by the individual chemicals or the mixture. Electron microscopic examination of the kidney showed an increase of single membrane vacuoles in the proximal convoluted tubules of rats treated with a mixture of chemicals, but not with **toluene** or styrene alone.
[Chakrabarti S, Tuchweber B; Toxicol Lett 39 (1): 27-34 (1987)]**PEER REVIEWED**

... **Toluene** has been shown to be a competitive inhibitor of the metabolism of benzene. This competitive interaction alleviates the metabolite-mediated toxicity of benzene ...
[Klaassen, C.D., M.O. Amdur, Doull J. (eds.). Casarett and Doull's Toxicology. The Basic Science of Poisons. 5th ed. New York, NY: McGraw-Hill, 1995. 741]**PEER REVIEWED**

Xenobiotic competitors for the same metabolic route, such as benzene and xylene, would ... have an impact on **toluene** metabolism.
[U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.95

(1994) ATSDR/TP-93/14]**PEER REVIEWED**

... A single alcoholic drink has a very strong, acute inhibitory effect on the hepatic elimination of **toluene**.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V71 842 (1999)]**PEER REVIEWED**

The aim of this study was to examine if the drug chlorzoxazone has any influence on the toxicokinetics of acetone and **toluene**. Chlorzoxazone is mainly metabolized by the same enzyme (Cytochrome P450 2E1) as ethanol and many other organic solvents. Ten male volunteers were exposed to solvent vapor (2 hr, 50 watt) in an exposure chamber. Each subject was exposed to acetone only (250 ppm), acetone + chlorzoxazone, **toluene** (50 ppm) only, **toluene** + chlorzoxazone, and chlorzoxazone only. Chlorzoxazone (500 mg) was taken as two tablets 1 h prior to solvent exposure. Samples of blood, urine and exhaled air were collected before, during and until 20 h post exposure. The time-concentration curves of acetone and **toluene** in blood were fitted to one- and four-compartment toxicokinetic models, respectively. Except for a delayed excretion of hippuric acid in urine, no effects on the **toluene** toxicokinetics were seen after chlorzoxazone treatment. Small increases in chlorzoxazone plasma levels were seen after exposure compared to chlorzoxazone alone. These interactions, although statistically significant, seem to be small compared to the interindividual variability on metabolism and toxicokinetics.
[Ernstgard L et al; Toxicol Sci 48 (2): 189-96 (1999)]**PEER REVIEWED**

TOLUENE

CASRN: 108-88-3

For other data, click on the Table of Contents

Pharmacology:

Interactions:

IP LD50 OF **TOLUENE** FOR MALE MICE WAS 1.15 G/KG. PRETREATMENT WITH PHENOBARBITAL, PRODUCED MARKED DECR IN SLEEP INDUCED BY TEST DOSE (0.96 G/KG IP) OF **TOLUENE**. PRETREATMENT WITH HEPATIC ENZYME INHIBITORS SUCH AS CARBON TETRACHLORIDE, 2-DIETHYLAMINOETHYL-2,2-DIPHENYLATE HYDROCHLORIDE, PYRAZOLE & CYANAMIDE PRODUCED INCR IN SLEEP & DEATH ASSOC WITH PROLONGATION OF SLEEPING TIME.
[KOGA K, OHMIYA Y; J TOXICOL SCI 3 (1): 25 (1978)]**PEER REVIEWED**

TOLUENE WITH ASPHALT FUMES OR CHLORINATED HYDROCARBONS, SUCH AS TRICHLOROETHYLENE & TETRACHLOROETHENE, CAUSES DEPRESSION OF HYDROXYLATION & URINARY CONJUGATE EXCRETIONS. ... COMBINED EXPOSURE TO **TOLUENE**, XYLENE, FORMALDEHYDE, & ANILINE DYES DECR GRANULOCYTIC PHOSPHATASE ACTIVITY. CONVERSELY, HYDROGEN PEROXIDE ADMIN TO RATS INCR THE BLOOD PEROXIDE ACTIVITY & INCR THE TOLERANCE TO **TOLUENE**, AS DID PHENOBARBITAL IN SPECIFIC QUANTITIES.
[Clayton, G. D. and F. E. Clayton (eds.). Patty's Industrial Hygiene and Toxicology: Volume 2A, 2B, 2C: Toxicology. 3rd ed. New York: John Wiley Sons, 1981-1982. 3289]**PEER REVIEWED**

SPRAGUE-DAWLEY RATS WERE EXPOSED BY INHALATION TO **TOLUENE** (500, 1500, & 3000 PPM) FOR 3 DAYS. **TOLUENE** INCR CONCN OF LIVER MICROSOMAL CYTOCHROME P-450. A DOSE-DEPENDENT INCR IN THE IN VITRO LIVER MICROSOMAL FORMATION OF SEVERAL METABOLITES OF BIPHENYL & BENZO(A)PYRENE WAS OBSERVED FOR **TOLUENE**. **TOLUENE** MODIFIED THE METABOLISM AND TOXICITY OF OTHER ENVIRONMENTAL CONTAMINANTS.
[TOFTGARD R ET AL; ACTA PHARMACOL TOXICOL 51 (2): 108 (1982)]**PEER REVIEWED**

Perchloroethylene enhances toxicity of **toluene** admin orally in rats.
[USEPA; Health Assessment Document: Toluene p.15-1 (1982) EPA-800/8-82-008]**PEER REVIEWED**

Toluene and trichloroethylene seem to exhibit competitive inhibition.
[Ikeda M; Int Arch Arbeitsmed 33 (2): 125 (1974)]**PEER REVIEWED**

CFY rats ... on day 12 of pregnancy ... dams were given: 0, 125, 250, 500 and 3,600 mg/cu m ... and 250 mg/kg acetylsalicylic acid by gavage; two subgroups ... treated with 250 mg/kg acetylsalicylic acid in combination with 3,600 mg/cu m **toluene** inhalation were given 0, 2.5, or 5 gm/kg glycine 2 hours before the acetylsalicylic acid dose. ... **Toluene** was found to potentiate the toxic effect of acetylsalicylic acid and to increase both maternal and embryonic toxicity ... increasing acetylsalicylic acid embryotoxicity

caused by **toluene** can be warded off by glycine administration.
[Ungvary G et al; Teratology 27 (2): 261-9 (1983)]**PEER REVIEWED**

The metabolic interaction of **toluene** and ethanol was studied in male rabbits having received ethanol (26.0 mmol/kg po), **toluene** (5.4 mmol/kg po) or both. Compared with ethanol alone, **toluene** given 2 hr after ethanol caused a significantly higher and more prolonged concentration of blood alcohol. A similar trend of blood alcohol was observed at the later stage with **toluene** given prior to ethanol. On the other hand, with simultaneous doses of the two substances, the blood **toluene** concentration was higher for the first 15-30 min than the ethanol control and the urinary excretion of hippuric acid, a main metabolite of **toluene**, was markedly decreased for the first 2 hr. The blood ethanol in this group, on the contrary, was reduced until 1 hr after administration. These results indicate that **toluene** and ethanol act reciprocally as competitive inhibitors in their metabolism after single administrations.
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[Chakrabarti S, Tuchweber B; Toxicol Lett 39 (1): 27-34 (1987)]**PEER REVIEWED**

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[Klaassen, C.D., M.O. Amdur, Doull J. (eds.). Casarett and Doull's Toxicology. The Basic Science of Poisons. 5th ed. New York, NY: McGraw-Hill, 1995. 741]**PEER REVIEWED**

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[U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.95 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

... A single alcoholic drink has a very strong, acute inhibitory effect on the hepatic elimination of **toluene**.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V71 842 (1999)]**PEER REVIEWED**

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[Ernstgard L et al; Toxicol Sci 48 (2): 189-96 (1999)]**PEER REVIEWED**

Minimum Fatal Dose Level:

Ingestion of approximately 60 ml (625 mg/kg) of **toluene** proved fatal for a while male mental patient.
[Ameno K et al; Forensic Sci Int 41: 255-60 (1989) as cited in U.S. Dept Health & Human Services/Agency for Toxic Substances & Disease Registry; Toxicological Profile for Toluene (Update) p.52 (1994) ATSDR/TP-93/14]**PEER REVIEWED**

TOLUENE

CASRN: 108-88-3

For other data, click on the Table of Contents

Environmental Fate & Exposure:

Environmental Fate/Exposure Summary:

Toluene is released into the atmosphere principally from the volatilization of petroleum fuels and **toluene**-based solvents and thinners and from motor vehicle exhaust. **Toluene**'s production and use as an intermediate in the production of benzoic acid, benzaldehyde, benzene, explosives, dyes and many other organic compounds may also result in its release to the environment through various waste streams. **Toluene** has been detected in emissions from volcanos, forest fires and crude oil. If released to air, a vapor pressure of 28.4 mm Hg at 25 deg C indicates **toluene** will exist solely as a vapor in the ambient atmosphere. Vapor-phase **toluene** will be degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals; the half-life for this reaction in air is estimated to be 3 days. **Toluene** may also be degraded in the atmosphere by reaction with nitrate radicals and ozone molecules, but these reactions are too slow to be environmentally important. If released to soil, **toluene** is expected to have high to moderate mobility based upon Koc values in the range of 37-178. Volatilization from moist soil surfaces is expected to be an important fate process based upon a Henry's Law constant of 6.64X10-3 atm-cu m/mole. **Toluene** may volatilize from dry soil surfaces based upon its vapor pressure. Biodegradation is expected to occur rapidly in soil surfaces, with half-lives in the range of several hours to 71 days. If released into water, **toluene** is not expected to adsorb to suspended solids and sediment based upon a Koc of 166 measured in lake sediment. Biodegradation is expected to occur rapidly in water, with reported half-lives of 4 and 56 days in aerobic and anaerobic water, respectively. Volatilization from water surfaces is expected to be an important fate process based upon this compound's Henry's Law constant. Estimated volatilization half-lives for a model river and model lake are 1 hour and 4 days, respectively. Measured BCF values of 13 and 90 in fish suggest bioconcentration in aquatic organisms is low to moderate. Hydrolysis is not expected to be an important environmental fate process for **toluene** due to lack of hydrolyzable functional groups. Exposure to **toluene** may occur occupationally during its production or subsequent use, particularly as a solvent or in gasoline, via dermal and respiratory routes. The main route of exposure for the general population will be through inhalation from contaminated air and handling of gasoline as well as ingestion of contaminated drinking water and food, and exposure to some consumer products. (SRC)
PEER REVIEWED

Probable Routes of Human Exposure:

NIOSH (NOES Survey 1981-1983) has statistically estimated that 1,625,598 workers (288,299 of these are female) are potentially exposed to **toluene** in the US(1). Occupational exposure to **toluene** may occur through inhalation and dermal contact with this compound at workplaces where **toluene** is produced or used(SRC). The general population may be exposed to **toluene** via inhalation of ambient air, ingestion of food and drinking water, handling of gasoline, and exposure to some consumer products where **toluene** is used as a solvent(SRC).
[(1) NIOSH; National Occupational Exposure Survey (NOES) (1983)]**PEER REVIEWED**

Toluene was detected in hairdresser salons in Norway at concns of 0.04-0.11 mg/cu m(1). The time weighted average (TWA) of **toluene** in the workplace air of a municipal waste composting facility was reported as 188,000 ug/cu m(2). In a 1989 Danish survey on chemical exposures(3), the number of worker exposure events for **toluene** were documented: manufacturing of metals, 420; manufacturing of metal fabricated products 64,000; electrical machinery and apparatus, 1,500; manufacture of transport equipment 2,700; painters and carpenters 15,000; construction workers, 5,400; publishing and printing, 6,300; wholesale trades, 5,000; textile and leather manufacturing, 4,400; wood and furniture manufacturing, 5,900; manufacture of chemicals, 8,700; manufacture of paints and petroleum, 1,400; manufacture of non-metallic mineral products, 2,300; manufacture of optical instruments, 2,500 manufacture of plastic and boat building, 1,100; sewage and refuse disposal, 99; agriculture and forestry, 11,000; health services, 2,600. The total number of work related exposure events was 140,000(3). **Toluene** was detected in the workplace air of glass fiber manufacturing plants and high temperature sealing component and clutch lining plants at a mean concn of 65 ppm(4).
[(1) Hollund BE, Moen BE; Ann Occup Hyg 42: 277-81 (1998) (2) Eitzer BD; Environ Sci Technol 29: 896-902 (1995) (3) Brandorff NP et al; Occup Environ Med 52: 454-63 (1995) (4) Angerer J, Kraemer A; Int Arch Occup Environ Health 69: 91-96 (1997)]**PEER REVIEWED**

Body Burden:

Toluene was identified, not quantified, in 8 samples of mothers' milk from 4 urban areas(1). **Toluene** was detected in 250 of 250 specimens of human blood at concns of 0.2-38 ppb (1.5 ppb avg)(2). **Toluene** was detected in 91% of the samples of the National Human Adipose Tissue Survey at a max concn of 250 ppb(3). **Toluene** was identified, not quantified, in expired breath of people at service stations during fueling(4). The mean concn of **toluene** in the blood of non-occupationally exposed individuals in the US was 0.52 ppb(5). The avg concn of **toluene** in the blood and urine of workers in glass fiber and clutch lining plants were 911 ug/l and 2.9 mg/l, respectively(6).
[(1) Pellizzari ED et al; Bull Environ Contam Toxicol 28: 322-8 (1982) (2) Antoine SR et al; Bull Environ Contam Toxicol 36: 364-71 (1986) (3) Stanley JS; Broad Scan Analysis of the FY82 National Human Adipose Tissue Survey Specimens Vol. I Executive Summary p. 5 USEPA-560/5-86-035 (1986) (4) Lindstrom AB, Pleil J; J Air Waste Manage Assoc 46: 676-82 (1996) (5) Ashley DL et al; Clin Chem 40: 1401-14 (1994) (6) Angerer J, Kraemer A; Int Arch Occup Environ Health 69: 91-96 (1997)]**PEER REVIEWED**

Average Daily Intake:

AIR INTAKE (assume median concn 11 ppb(1)) 843 ug; WATER INTAKE (assume 2 ppb(2)) 4 ug; FOOD INTAKE - insufficient data.
[(1) Brodzinsky R, Singh HB; Volatile Organics in the Atmosphere and Assessment of available data: p. 126-7 SRI Contract 68-02-3459 (1982) (2) Otson R et al; J Assoc Off Analyt Chem 65: 1370-4 (1982)]**PEER REVIEWED**

Natural Pollution Sources:

Toluene occurs in nature in ... natural gas deposits ...

[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47 82 (1989)]**PEER REVIEWED**

Toluene has been detected in emissions from volcanos, forest fires and crude oil(1).
[(1) Graedel TE; Chemical Compounds in the Atmosphere, NY, NY, Academic Press p. 108 (1978)]**PEER REVIEWED**

Artificial Pollution Sources:

Toluene is a major constituent (20-60 ug/cigarette) of the gas phase of the mainstream smoke of unfiltered cigarettes. /From table/
[Rom, W.N. (ed.). Environmental and Occupational Medicine. 2nd ed. Boston, MA: Little, Brown and Company, 1992. 1212]**PEER REVIEWED**

Toluene is released into the atmosphere principally from the volatilization of petroleum fuels and **toluene**-based solvents and thinners and from motor vehicle exhaust(1,2). **Toluene**'s production and use as an intermediate in the production of benzoic acid, benzaldehyde, explosives, dyes and many other organic compounds(3) may also result in its release to the environment through various waste streams(SRC).
[(1) Graedel TE; Chemical Compounds in the Atmosphere. NY, NY: Academic Press p. 108 (1978) (2) Walker P; Air Pollution Assessment of Toluene. TR-7215 Mitre Corp, McLean VA, pp. 1-22, 46-92 (1976) (3) Budvari S; Merck Index, 12th ed, Whitehouse Station, NJ Merck & Co. p 1626 (1996)]**PEER REVIEWED**

Environmental Fate:

TERRESTRIAL FATE: Based on a classification scheme(1), Koc values of 37-178 measured in soil(2,3), indicates that **toluene** is expected to have high to moderate mobility in soil(SRC). Volatilization of **toluene** from moist soil surfaces is expected to be an important fate process(SRC) given a Henry's Law constant of 6.64X10-3 atm-cu m/mole(4). **Toluene** may volatilize from dry soil surfaces based on a vapor pressure of 28.4 mm Hg at 25 deg C(5). Complete biodegradation of **toluene** was observed in lab microcosm tests during a 40 hour incubation period using soils previously exposed to **toluene**(6). The biodegradation half-life in various soils was reported as several hours to 71 days(7).
[(1) Swann RL et al; Res Rev 85: 17-28 (1983) (2) Wilson JT et al; J Environ Qual 10: 501-6 (1981) (3) Nathwani JS, Phillips CR; Chemosphere 6: 157-62 (1977) (4) Mackay D et al; Environ Sci Technol 13: 333-36 (1979) (5) Daubert TE, Danner RP; Physical and Thermodynamic Properties of Pure Chemicals Data Compilation Washington, DC: Taylor and Francis (1989) (6) Allen-King RM et al; Environ Toxicol Chem 13: 693-705 (1994) (7) Aronson D et al; Aerobic biodegradation of organic chemicals in environmental media: a summary of field and laboratory studies. USEPA (1999)]**PEER REVIEWED**

AQUATIC FATE: Based on a classification scheme(1), a Koc value of 166 measured in lake sediment(2) indicates that **toluene** is not expected to adsorb to suspended solids and sediment(SRC). Volatilization

from water surfaces is expected(3) based upon a Henry's Law constant of 6.64X10-3 atm-cu m/mole(4). Using this Henry's Law constant and an estimation method(3), volatilization half-lives for a model river and model lake are 1 hour and 4 days, respectively(SRC). According to a classification scheme(5), BCF values of 13(6) and 90(7) measured in fish, suggest bioconcentration in aquatic organisms is low to moderate. The half-life of **toluene** in aerobic and anaerobic water was reported as 4 and 56 days, respectively(8).
[(1) Swann RL et al; Res Rev 85: 17-28 (1983) (2) Kan AT et al; Environ Sci Technol 32: 892-902 (1998) (3) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington, DC: Amer Chem Soc pp. 4-9, 15-1 to 15-29 (1990) (4) Mackay D et al; Environ Sci Technol 13: 333-36 (1979) (5) Franke C et al; Chemosphere 29: 1501- 14 (1994) (6) Ogata M, Miyake Y; Water Res 12: 1041-4 (1978) (7) Freitag D et al; Chemsophere 14: 1589-1616 (1985) (8) Capel PD, Larson SL; Chemosphere 30: 1097-1107 (1995)]**PEER REVIEWED**

ATMOSPHERIC FATE: According to a model of gas/particle partitioning of semivolatile organic compounds in the atmosphere(1), **toluene**, which has a vapor pressure of 28.4 mm Hg at 25 deg C(2), is expected to exist solely as a vapor in the ambient atmosphere. Vapor-phase **toluene** is degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals, nitrate radicals and ozone molecules(SRC). The half-life for the reaction with hydroxyl radicals is estimated to be 3 days(SRC), calculated from its rate constant of 5.96X10-12 cu cm/molecule-sec at 25 deg C(3). The half-life for the nighttime reaction with nitrate radicals is estimated as 491 days(SRC) calculated from its rate constant of 6.8X10-17 cu cm/molecule-sec at 25 deg C(3). The half-life for the reaction with ozone is estimated as 27,950 days(SRC) calculated from its rate constant of 4.1X10-22 cu cm/molecule-sec at 25 deg C(3).
[(1) Bidleman TF; Environ Sci Technol 22: 361-367 (1988) (2) Daubert TE, Danner RP; Physical and Thermodynamic Properties of Pure Chemicals Data Compilation Washington, DC: Taylor and Francis (1989)(3) Atkinson R; J Phys Chem Ref Data Monograph 2 (1994)]**PEER REVIEWED**

Environmental Biodegradation:

Toluene is readily degradable in a variety of standard biodegradability tests using sewage seed or sludge inoculums(1-7). Degradation has been observed in several die-away tests using seawater or estuarine water(9-12). The degradation rate is much faster in systems which have been contaminated by oil(9,10). Complete degradation has been observed in 4 days and 22 days in a marine mesocosm with summer and spring conditions, respectively(12), and 10 days in a 1% gas oil mixture in a North Sea coast water inoculum(8). A 90 day half-life in uncontaminated estuarine water was reduced to 30 days in oil-polluted water(10). The half-life in water collected near Port Valdez, Alaska was 12 days(9). 1.5 mM and 3 mM Ring-labeled **toluene** added to a methanogenic inoculum originally enriched from sewage sludge and incubated at 35 deg C for 60 days resulted in 3.6 and 4.5% 14-C final activity respectively(13).
[(1) Tabak HH et al; J Water Pollut Control Fed 53: 1503-8 (1981) (2) Davis EM et al; Water Res 15: 1125-7 (1981) (3) Bridie AL et al; Water Res 13: 627-30 (1979) (4) Kawasaki M; Ecotox Environ Safety 4: 444-54 (1980) (5) Malaney GW, McKinney RE; Water Sewage Works 113: 302-9 (1966) (6) Price KS et al; J Water Pollut Control Fed 46: 63-77 (1974) (7) Matsui S et al; Prog Water Technol 7: 645-59 (1975) (8) Van der Linden AC; Dev Biodegrad Hydrocarbons 1: 165-200 (1978) (9) Button DK

et al; Appl Environ Microbiol 42: 708-19 (1981) (10) Lee RF; 1977 Oil Spill Conf Amer Petrol Inst p 611-6 (1977) (11) Reichardt PB et al; Environ Sci Technol 15: 75-9 (1981) (12) Wakeham SG et al; Environ Sci Technol 17: 611-7 (1983) (13) Grbic-Galic D, Vogel TM; Appl Environ Microbiol 53: 254-60 (1987)]**PEER REVIEWED**

Toluene completely degraded in groundwater in 8 days including a lag of 3-4 days while microbial populations became acclimated(1). Other investigators found that only 1-2% of **toluene** degraded in the subsurface environment(2) and >90% degraded in 4 weeks in soil cores at various depths both above and below the water table(3,5). Microbial attack proceeds via immediate hydroxylation of the benzene ring followed by ring-cleavage or oxidation of the side chain followed by hydroxylation and ring-cleavage(4).
[(1) Kappeler T, Wuhrmann K; Water Res 12: 327-33 (1978) (2) Wilson JT et al; Devel Indust Microbiol 24: 225-33 (1983) (3) McNabb JF et al; 81st Ann Mtg Amer Soc Microbiology p.213 (1981) (4) Fewson CA; FEMS Symp 12 (Microb Deg Xenobiotics Recalcitrant Cmpds): 141-79 (1981) (5) Wilson JT et al; Ground Water 21: 134-42 (1983)]**PEER REVIEWED**

Complete biodegradation of **toluene** was observed in lab microcosm tests during a 40 hour incubation period using soils previously exposed to **toluene**(1). **Toluene** was rapidly degraded in soil column experiments using acclimated soil at a rate of 8-35 mg/kg-day, and the rate followed zero-order kinetics(2). First-order degradation rate constants of 0.0005 to 0.0063 day-1 were measured for **toluene** in a gasoline-contaminated aquifer zone(3). These rate constants correspond to half-lives of 100-1,386 days(3). A first-order biodegradation rate constant of 0.045 day-1 was reported for **toluene** in an anaerobic petroleum contaminated aquifer, corresponding to a biodegradation half-life of 15 days(4). **Toluene** was rapidly biodegraded by indigenous mixed cultures in sandy aquifer material and pure cultures isolated from the aquifer(5). The zero-order rate constant for the aquifer material was 23 mg/l-day and had a lag period of 2 days(5). The half-life of **toluene** in aerobic and anaerobic water was reported as 4 and 56 days, respectively(6). The biodegradation half-life in various soils was reported as several hours to 71 days(7).
[(1) Allen-King RM et al; Environ Toxicol Chem 13: 693-705 (1994) (2) Allen-King RM et al; J Environ Qual 25: 287-95 (1996) (3) Borden RC et al; Water Resour Res 33: 1105-15 (1997) (4) Borden RC et al; Anaerobic Biodegradation of BTEX in Aquifer Material USEPA/600/S-97/003. National Risk Management Laboratory, Ada, OK. pp. 9 (1997) (5) Alvarez PJJ, Vogel TM; Appl Environ Microbiol 57: 2981-85 (1991) (6) Capel PD, Larson SL; Chemosphere 30: 1097-1107 (1995) (7) Aronson D et al; Aerobic biodegradation of organic chemicals in environmental media: a summary of field and laboratory studies. USEPA (1999)]**PEER REVIEWED**

Environmental Abiotic Degradation:

The rate constant for the vapor-phase reaction of **toluene** with photochemically-produced hydroxyl radicals has been measured as 5.96X10-12 cu cm/molecule-sec at 25 deg C(1). This corresponds to an atmospheric half-life of about 3 days at an atmospheric concentration of 5X10+5 hydroxyl radicals per cu cm(1). The rate constant for the vapor-phase reaction of **toluene** with nitrate radicals has been measured as 6.8X10-17 cu cm/molecule-sec at 25 deg C(1). This corresponds to an atmospheric half-life

of about 491 days at an atmospheric concentration of 2.4X10+8 nitrate radicals per cu cm(2). The rate constant for the vapor-phase reaction of **toluene** with ozone has been measured as 4.1X10-22 cu cm/molecule-sec at 25 deg C(1). This corresponds to an atmospheric half-life of about 27,950 days at an atmospheric concentration of 7X10+11 ozone molecules per cu cm(3). **Toluene** is not expected to undergo hydrolysis in the environment due to the lack of hydrolyzable functional groups(4) nor to directly photolyze due to the lack of absorption in the environmental UV spectrum.
[(1) Atkinson R; J Phys Chem Ref Data Monograph 2 (1994) (2) Atkinson R et al; Atmos Environ 24: 2647-54 (1990) (3) Atkinson R, Carter WPL; Chem Rev 84: 437-70 (1984) (4) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington, DC: Amer Chem Soc pp. 7-4, 7-5 (1990)]**PEER REVIEWED**

Environmental Bioconcentration:

The BCF of **toluene** in eels was reported as 13(1) and the BCF in golden ide was reported as 90(2). According to a classification scheme(3), this BCF data suggests bioconcentration in aquatic organisms is low to moderate.
[(1) Ogata M, Miyake Y; Water Res 12: 1041-4 (1978) (2) Freitag D et al; Chemosphere 14: 1589-1616 (1985) (3) Franke C et al; Chemosphere 29: 1501-14 (1994)]**PEER REVIEWED**

Soil Adsorption/Mobility:

In association with clay minerals, **toluene**'s adsorption is inversely proportional to the pH of the soil. Approximately 40-70% of **toluene** applied to the surface of sandy soils is volatilized.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47 90 (1989)]**PEER REVIEWED**

The Koc of **toluene** was reported as 178 in a sandy soil(1) and as 37 (Wendover silty loam), 160 (Grimsby silt loam), 160 (Vaudreil sandy loam) and 46 (sandy soil)(2). The Koc of **toluene** in lake sediment was measured as 166(3). According to a classification scheme(4), this Koc data suggests that **toluene** is expected to have high to moderate mobility in soil.
[(1) Wilson JT et al; J Environ Qual 10: 501-6 (1981) (2) Nathwani JS, Phillips CR; Chemosphere 6: 157-62 (1977) (3) Kan AT et al; Environ Sci Technol 32: 892-902 (1998) (4) Swann RL et al; Res Rev 85: 17-28 (1983)]**PEER REVIEWED**

Volatilization from Water/Soil:

The Henry's Law constant for **toluene** is 6.64X10-3 atm-cu m/mole(1). This Henry's Law constant indicates that **toluene** is expected to volatilize rapidly from water surfaces(2). Based on this Henry's Law constant, the volatilization half-life from a model river (1 m deep, flowing 1 m/sec, wind velocity of 3 m/sec)(2) is estimated as 1 hour(SRC). The volatilization half-life from a model lake (1 m deep, flowing 0.05 m/sec, wind velocity of 0.5 m/sec)(2) is estimated as 4 days(SRC). **Toluene**'s Henry's Law constant(1) indicates that volatilization from moist soil surfaces may occur(SRC). **Toluene** may volatilize from dry soil surfaces based upon a vapor pressure of 28.4 mm Hg at 25 deg C(3).

[(1) Mackay D et al; Environ Sci Technol 13: 333-36 (1979) (2) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington, DC: Amer Chem Soc pp. 15-1 to 15-29 (1990) (3) Daubert TE, Danner RP; Physical and Thermodynamic Properties of Pure Chemicals Data Compilation Washington, DC: Taylor and Francis (1989)]**PEER REVIEWED**

Environmental Water Concentrations:

Toluene is detected in 28% of National Priority List (NPL) sites in groundwater. Average concentration: 5.18 ppm; Maximum concentration: 1100 ppm. /From table/
[Sullivan, J.B. Jr., G.R. Krieger (eds.). Hazardous Materials Toxicology-Clinical Principles of Environmental Health. Baltimore, MD: Williams and Wilkins, 1992. 304]**PEER REVIEWED**

GROUNDWATER: **Toluene** was detected in groundwater near contaminated wells from gasoline storage tanks at concns of 0.55-6400 ppb(1,2) and groundwater underlying 2 rapid infiltration sites at 0.2 ppb(3). Groundwater under a gasification site 15 months after gasification contained **toluene** at 170-740 ppb(4). In a cluster well study under an old industrial site, mean levels of **toluene** in bedrock wells were 90 ppb while shallow and deep glacial wells were 10 ppb(5). **Toluene** was detected in 1.3% of the samples in the US Ground Water Supply Survey, 1982, at a max concn of 2.9 ppb and a median concn of 0.8 ppb(6).
[(1) Burmaster DE; Environ 24: 6-13, 33-6 (1982) (2) Tester DJ, Harker RJ; Water Pollut Control 80: 614-31 (1981) (3) Hutchins SR et al; Environ Toxicol Chem 2: 195-216 (1983) (4) Stuermer DH et al; Environ Sci Technol 16: 582-7 (1982) (5) Rich CA; Stud Environ Sci 17(Qual Groundwater): 309-14 (1981) (6) Coturvo JA; Sci Total Environ 47: 7-26 (1985)]**PEER REVIEWED**

DRINKING WATER: **Toluene** was detected in 33% of the samples from 30 Canadian treatment facilities at an avg concn of 2 ppb (14 ppb max) in summer months and in 53% of the samples at an avg concn of <1 ppb (13 ppb max), during winter(1). **Toluene** was detected at concns of 0-2 ppb in drinking water of cities supplied by the Great Lakes(2). **Toluene** was detected in 14% of the samples of drinking water in the US at concns of less than 1 part per trillion(3). In a federal survey of finished drinking water from groundwater sources **toluene** was detected in less than 5% of the samples(4). **Toluene** was detected in 3 New Orleans area water supplies at 0-10 ppb(5). **Toluene** was identified, not quantified, in 60% of drinking water tested in the National Organics Reconnaissance Survey(6). The max concn of **toluene** in tapwater derived from bank-filtered Rhine River water was 1 ppb(7). **Toluene** was detected in 3 contaminated drinking water wells in New Jersey at 55, 260, 6400 ppb whereas the highest concn in drinking water from surface water sources was 6.1 ppb(8). Drinking water supplied from groundwater in England 210 m from a gasoline storage tank contained 0.15 ppb of **toluene**(9). In a 5-city survey in which the water supplies came from different types of sources with various sources of pollution, 2 contained **toluene**, one 0.1 ppb and the other 0.7 ppb(10). **Toluene** was detected in 20 of 182 bottled water samples at an avg concn of 6.92 ug/kg and a range of 0.5-63 ug/kg(11).
[(1) Otson R et al; J Assoc Off Analyt Chem 65: 1370-4 (1982) (2) Williams DT et al; Chemosphere 11: 263-76 (1982) (3) NAS; The Alkyl Benzene USEPA Contract No. 68-02-4655 (1980) (4) Dyksen JE, Hess AF

III: J Amer Water Works Assoc 74: 394-403 (1982) (5) Keith LH et al; pp. 329-73 in Identification and analysis of organic pollutants in Water, Keith LH, ed, Ann Arbor Sci Publ (1976) (6) Bedding ND et al; Sci Total Environ 25: 143-67 (1982) (7) Piet GJ, Morra CF; pp. 31-42 in Artificial Groundwater Recharge (Water Res Eng Ser) Huisman L, Olsthorn TN, eds, Pitman Publ (1983) (8) Burmaster DE; Environ 24: 6-13, 33-6 (1982) (9) Tester DJ, Harker RJ; Water Pollut Control 80: 614-31 (1981) (10) Coleman WE et al; pp. 305-27 in Analysis and identification of organic substances in water. Keith L, ed, Ann Arbor, MI: Ann Arbor Sci (1976) (11) Page RD et al; J AOAC Int 76: 26-31 (1993)]**PEER REVIEWED**

SURFACE WATER: **Toluene** was detected in 31 of 204 sites at concns of 1-5 ppb in 14 heavily industrialized river basins in the US(1). **Toluene** was identified, not quantified, in various rivers(2-5). **Toluene** was detected in the Gulf of Mexico at 3-376 parts per trillion(6,7) and the Vineland Sound, MA at 10-54 parts per trillion(8). **Toluene** was detected in the Elbe River, Germany at concns of 30-243 ng/l(9).
[(1) Ewing BB et al; Monitoring to detect previously unrecognized pollutants in surface waters USEPA 560/6-77-015 (appendix USEPA 560/6-77-015a) (1977) (2) Sheldon LS, Hites RA; Environ Sci Technol 12: 1188-94 (1978) (3) Goodley PC, Gordon M; KY Acad Sci 37: 11-5 (1976) (4) Zuercher F, Giger W; Vom Wasser 47: 37-55 (1976) (5) Zou H et al; Wat Res 30: 2003-2008 (1996) (6) Sauer TC Jr; Org Geochem 3: 91-101 (1981) (7) Sauer TC Jr et al; Mar Chem 7: 1-16 (1978) (8) Gschwend PM et al; Environ Sci Technol 16: 31-8 (1982) (9) Gotz R et al; Chemosphere 36: 2103-18 (1998)]**PEER REVIEWED**

RAIN WATER: **Toluene** was detected in rain in west Los Angeles at 76 parts per trillion(1). **Toluene** was detected in 71.4% of the rain samples from 7 rain events in Portland, OR, Feb-Apr 1984, at concns of 40-220 parts per trillion(2).
[(1) Kawamura K, Kaplan IR; Environ Sci Technol 17: 497-501 (1983) (2) Ligocki MP et al; Atmos Environ 19: 1609-17 (1985)]**PEER REVIEWED**

Effluent Concentrations:

Industries in which the mean effluent levels exceed 1000 ppb are: auto and other laundries, iron and steel manufacturing, gum and wood chemicals, pharmaceuticals, organic chemicals/plastics manufacturing, paint and ink formulation. The highest mean value is 52 ppm for pharmaceuticals and the highest maximum values are 230 and 260 ppm for pharmaceuticals and organic chemicals/plastics manufacturing(1). **Toluene** was detected in a plume from General Motors Paint Plant, Janesville, WI at 156 ppb(2). Auto exhaust contained **toluene** at concns of 196-718 mg/cu m(3).
[(1) USEPA; Treatability Manual p. I.9.10-1 to I.9.10-5 USEPA 600/2-82-001a (1981) (2) Sexton K, Westberg H; Environ Sci Technol 14: 329-32 (1980) (3) Tsani-Bazaca E et al; Environ Technol Lett 2: 303-16 (1981)]**PEER REVIEWED**

Toluene was detected in landfill gas emissions at concns of 20,400 ppb, 34,907 ppb and 76,700 ppb(1).

Toluene was detected in the gas emissions of 7 waste disposal sites in the UK at concns of 10-287 mg/cu m(2). **Toluene** was identified, not quantified, in the exhaust of a moped(3) and 4-stroke lawn mower(4). **Toluene** was detected in car exhaust under normal operating conditions at concns of 3.31-4.52 ppm and an avg of 3.83 ppm(5). The mean emission rate of **toluene** is 89-453 mg/km, with the lowest emission rates occurring at higher driving speeds(5). **Toluene** was detected in the effluent of a hazardous waste incinerator in Germany at a concn of 34 ug/cu m(6).
[(1) Brosseau J, Heitz M; Atmos Environ 28: 285-93 (1994) (2) Allen MR et al; Environ Sci Technol 31: 1054-61 (1997) (3) Ostermark U, Petersson G: Chemosphere 27: 1719-28 (1993) (4) Gabele P; J air Waste Manage Assoc 47: 945-52 (1997) (5) Baily JC et al; Atmos Environ 24A: 43-52 (1990) (6) Jay K, Stiegltz L; Chemosphere 30: 1249-60 (1995)]**PEER REVIEWED**

Sediment/Soil Concentrations:

SEDIMENT: **Toluene** was identified, not quantified in sediment from rivers near industrial facilities in the US(1,2). USEPA STORET DATABASE: **Toluene** was detected in 67 of 397 sediment samples at a median concn of 5.0 ppb dry weight(3). **Toluene** was detected in 33% of the sediment samples from Lake Pontchartrain, LA at an avg concn of 0.7 ppb wet weight(4). **Toluene** was detected at concns of less than 0.1 ng/g to 1.2 ng/g in sediment from rivers near Niigata, Japan(5). **Toluene** was detected in sediment of the Passaic River, NJ at concns of 3-250 ug/kg(6).
[(1) Goodley PC, Gordon M; KY Acad Sci 37: 11-5 (1976) (2) Steinheimer TR et al; Anal Chim Acta 129: 57-67 (1981) (3) Staples CA et al; Environ Toxicol Chem 4: 131-42 (1985) (4) Ferrario JB et al; Bull Environ Contam Toxicol 34: 246-55 (1985) (5) Kawata K et al; Bull Environ Contam Toxicol 58: 893-900 (1997) (6) Iannuzzi TJ et al; Chemosphere 34: 213-31 (1997)]**PEER REVIEWED**

Atmospheric Concentrations:

URBAN/SUBURBAN: In a survey of 3,195 samples obtained from urban areas in the US, **toluene** was detected at concns of 0-85 ppb (11 ppb median)(1). Average **toluene** concns in US cities range from 0.8-37 ppb with max values ranging from 6.5-1,110 ppb(2-9). Daily variations in concentrations and ratios of **toluene** to benzene indicate that auto traffic is the most common source of atmospheric **toluene**(10,11,12). **Toluene** was detected in Middelsbrough, UK and London, UK at 1.55 and 7.475 ppb, respectively(13). The avg concn of **toluene** inside buses and cars in Taipei, Taiwan was reported as 367 and 599 ug/cu m(14). **Toluene** was detected in various streets in Europe at concns of 87-127 ug/cu m(15). The concn of **toluene** inside automobiles in Paris, France was 178-258 ug/cu m(16).
[(1) Brodzinsky R, Singh HB; Volatile Organics in the Atmosphere: An Assessment of Available Data. p 126-7 SRI contract 68-02-3459 (1982) (2) Singh HB et al; Atmospheric measurements of Selected Hazardous Organic Chemicals USEPA 600/53-81-032 (1981) (3) Altshuller AP et al; Environ Sci Technol 5: 1009-16 (1971) (4) Singh HB et al; Atmos Environ 15: 601-12 (1981) (5) Arnts RR, Meeks SA; Biogenic hydrocarbon contribution to the ambient air of selected areas 128 USEPA 600/3-80-023 (1980) (6) Bozzelli JW et al; Analysis of selected toxic and carcinogenic substances in ambient air in New Jersey, NJ Dept

Environ Protect (1980) (7) Lonneman WA et al; Hydrocarbons in Houston air. USEPA 600/3-79-018 pp. 44 (1979) (8) Lioy PJ et al; J Water Pollut Control Fed 33: 649-57 (1983) (9) Pilar S, Graydon WF; Environ Sci Technol 7: 628-71 (1973) (10) Termonia M; Comm Eur Comm EUR 7624 pp. 356-61 (1982) (11) Sexton K, Westberg H; Environ Sci Technol 14: 329-32 (1980) (12) Tsani-Bazaca E et al; Chemosphere 11: 11-23 (1982) (13) Derwent RG; pp. 1-15 in Volatile Organic Compounds in the Atmosphere. Hester RE, Harrison RM, Iss Environ Sci Technol No 4, the Royal Society of Chemistry, Cambridge, UK (1995) (14) Chan CC et al; Atmos Environ 28: 2351-59 (1994) (15) Coursimault A et al; Sci Total Environ 169: 17-23 (1995) (16) Dor F et al; J Air Waste Manage Assoc 45: 103-110 (1995)]**PEER REVIEWED**

INDOOR AIR: **Toluene** was detected at mean concns of 4.8 ug/cu m in telephone communications offices, 10.1 ug/cu m in data center offices and 5.7 ug/cu m in administrative offices in the US(1). **Toluene** was detected in the volatile emissions of newly installed carpet cushions at an emission rate of 4-79 ug/sq m-hr during the first 6 hours after installation(2). **Toluene** was detected in hairdresser salons in Norway at concns of 0.04-0.11 mg/cu m(3).
[(1) Shields HC et al; Indoor air 6: 2-17 (1996) (2) Schaeffer VH et al; J Air Waste Manage Assoc 46: 813-20 (1996) (3) Hollund BE, Moen BE; Ann Occup Hyg 42: 277-81 (1998)]**PEER REVIEWED**

RURAL/REMOTE: **Toluene** was detected in the atmosphere of 115 remote samples taken in the US at concns of 0.057-30 ppb, (0.66 ppb median)(1). **Toluene** was identified, not quantified, in a forest in Germany(2). **Toluene** was detected in Langenbrugge, Germany and West Beckham, UK at concns of 0.441 and 0.999 ppb, respectively(3). **Toluene** was detected at a concn of 0.04 ppb in Izana, Canaries(3)
[(1) Brodzinsky R, Singh HB; Volatile Organics in the Atmosphere: An Assessment of Available Data. pp. 126-7 SRI contract 68-02-3459 (1982) (2) Helmig D et al; Chemosphere 19: 1399-1412 (1989) (3) Derwent RG; pp. 1-15 in Volatile Organic Compounds in the Atmosphere, Hester RE, Harrison RM. Iss Environ Sci Technol No 4, the Royal Society of Chemistry, Cambridge, UK (1995)]**PEER REVIEWED**

SOURCE DOMINATED: In a survey of 188 source dominated samples from the US, **toluene** was detected at concns of 0.037-5,500 ppb (4.6 ppb median)(1). **Toluene** was detected in the air of the Lipari and BFI landfills in NJ at 0.40 and 310 ppb(2). **Toluene** was detected at concns of 14-22 ppb 4 miles downwind from a General Motors paint plant(3). The avg concn of **toluene** around gasoline pumps during fueling was in the range of 0.14-1.2 mg/cu m and the fenceline concns at the filling stations were in the range of 0.005-0.02 ppm(4). **Toluene** was detected in the Fort McHenry Tunnel, MD at concns of 79-90 ppb(5).
[(1) Brodzinsky R, Singh HB; Volatile Organics in the Atmosphere: An Assessment of Available Data. pp. 126-7 SRI contract 68-02-3459 (1982) (2) Bozzelli JW et al; Analysis of selected toxic and carcinogenic substances in ambient air in New Jersey, NJ Dept Environ Protect (1980) (3) Tsani-Bazaca E et al; Chemosphere 11: 11-23 (1982) (4) American Petroleum Inst; Gasoline Vapor Exposure Assessment at Service Stations. American Petroleum Inst Washington, DC: API Publ 4553 (1993)

(5) Zielinska B et al; Atmos Environ 12: 2269-86 (1996)]**PEER REVIEWED**

Food Survey Values:

Toluene was identified, not quantified, in baked potatoes(1), mountain cheese(2), fried bacon(3), fried chicken(4), peanut oil(5) and raw beef(6).
[(1) Coleman EC et al; J Agric Food Chem 29: 42-8 (1981) (2) Dumont JP, Adda J; J Agric Food Chem 26: 364-7 (1978) (3) Ho CT et al; J Agric Food Chem 31: 336-42 (1983) (4) Tang JT et al; J Agric Food Chem 31: 1287-92 (1983) (5) Chung TY et al; J Agric Food Chem 41: 1467-70 (1993) (6) King MF et al; J Agric Food Chem 41: 1974-81 (1993)]**PEER REVIEWED**

Plant Concentrations:

Toluene was identified, not quantified, in the Korean Chamachwi plant(1).
[(1) Chung TY et al; J Agric Food Chem 41: 1693-97 (1993)]**PEER REVIEWED**

Fish/Seafood Concentrations:

Flesh of fish from petroleum contaminated harbor in Japan contained **toluene** at 5 ppm(1). **Toluene** was detected in oysters from Lake Pontchartrain, LA at an avg concn of 3.4 ppb and clams at concns of 18 and 11 ppb(2). **Toluene** was identified, not quantified, in boiled shrimp and crab(3).
[(1) USEPA; Ambient Water Quality Criteria for Toluene. pp. C-1 to C-7 (1980) (2) Ferrario JB et al; Bull Environ Contam Toxicol 34: 246-55 (1985) (3) Misharina TA, Golovnya RV; J High Resol Chromat 15: 332-34 (1992)]**PEER REVIEWED**

Milk Concentrations:

Toluene was identified, not quantified, in 8 samples of mothers' milk from 4 urban areas(1).
[(1) Pellizzari ED et al; Bull Environ Contam Toxicol 28: 322-8 (1982)]**PEER REVIEWED**

Other Environmental Concentrations:

Light oil from coal 12-20% **toluene**; crude oil 1.2-2.4% auto fuel 8-12%(1).
[(1) Walker P; Air Pollution Assessment of Toluene. p. 1-22, 46-92 MTR-7215 Mitre Corp, McLean VA (1976)]**PEER REVIEWED**

Evaporation from gasoline tank: 0.3 - 0.9 vol % of total evaporated hydrocarbons; evaporation from carburetor: 0.5 - 2.4 vol % of total evaporated hydrocarbons.
[Verschueren, K. Handbook of Environmental Data on Organic Chemicals. 3rd ed. New York, NY: Van Nostrand Reinhold Co., 1996. 1723]**PEER REVIEWED**

In exhaust of gasoline engines: 3-8 vol% of total exhaust hydrocarbons; in exhaust of diesel engine: 3% of emitted hydrocarbons; in exhaust of rotary gasoline engine: 16% of emitted hydrocarbons; in exhaust

of gasoline engine: 0.1-7.0 ppm (partly crotonaldehyde); in 4 municipal landfill gases in S. Finland (1989-1990): avg 0.23-137, max 143 mg/cu m.
[Verschueren, K. Handbook of Environmental Data on Organic Chemicals. 3rd ed. New York, NY: Van Nostrand Reinhold Co., 1996. 1723]**PEER REVIEWED**

TOLUENE

CASRN: 108-88-3

For other data, click on the Table of Contents

Environmental Fate/Exposure Summary:

Toluene is released into the atmosphere principally from the volatilization of petroleum fuels and **toluene**-based solvents and thinners and from motor vehicle exhaust. **Toluene**'s production and use as an intermediate in the production of benzoic acid, benzaldehyde, benzene, explosives, dyes and many other organic compounds may also result in its release to the environment through various waste streams. **Toluene** has been detected in emissions from volcanos, forest fires and crude oil. If released to air, a vapor pressure of 28.4 mm Hg at 25 deg C indicates **toluene** will exist solely as a vapor in the ambient atmosphere. Vapor-phase **toluene** will be degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals; the half-life for this reaction in air is estimated to be 3 days. **Toluene** may also be degraded in the atmosphere by reaction with nitrate radicals and ozone molecules, but these reactions are too slow to be environmentally important. If released to soil, **toluene** is expected to have high to moderate mobility based upon Koc values in the range of 37-178. Volatilization from moist soil surfaces is expected to be an important fate process based upon a Henry's Law constant of 6.64X10-3 atm-cu m/mole. **Toluene** may volatilize from dry soil surfaces based upon its vapor pressure. Biodegradation is expected to occur rapidly in soil surfaces, with half-lives in the range of several hours to 71 days. If released into water, **toluene** is not expected to adsorb to suspended solids and sediment based upon a Koc of 166 measured in lake sediment. Biodegradation is expected to occur rapidly in water, with reported half-lives of 4 and 56 days in aerobic and anaerobic water, respectively. Volatilization from water surfaces is expected to be an important fate process based upon this compound's Henry's Law constant. Estimated volatilization half-lives for a model river and model lake are 1 hour and 4 days, respectively. Measured BCF values of 13 and 90 in fish suggest bioconcentration in aquatic organisms is low to moderate. Hydrolysis is not expected to be an important environmental fate process for **toluene** due to lack of hydrolyzable functional groups. Exposure to **toluene** may occur occupationally during its production or subsequent use, particularly as a solvent or in gasoline, via dermal and respiratory routes. The main route of exposure for the general population will be through inhalation from contaminated air and handling of gasoline as well as ingestion of contaminated drinking water and food, and exposure to some consumer products. (SRC)

PEER REVIEWED

TOLUENE

CASRN: 108-88-3

For other data, click on the Table of Contents

Natural Pollution Sources:

Toluene occurs in nature in ... natural gas deposits ...
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47 82 (1989)]**PEER REVIEWED**

Toluene has been detected in emissions from volcanos, forest fires and crude oil(1).
[(1) Graedel TE; Chemical Compounds in the Atmosphere, NY, NY, Academic Press p. 108 (1978)]**PEER REVIEWED**

TOLUENE

CASRN: 108-88-3

For other data, click on the Table of Contents

Artificial Pollution Sources:

Toluene is a major constituent (20-60 ug/cigarette) of the gas phase of the mainstream smoke of unfiltered cigarettes. /From table/

[Rom, W.N. (ed.). Environmental and Occupational Medicine. 2nd ed. Boston, MA: Little, Brown and Company, 1992. 1212]**PEER REVIEWED**

Toluene is released into the atmosphere principally from the volatilization of petroleum fuels and **toluene**-based solvents and thinners and from motor vehicle exhaust(1,2). **Toluene**'s production and use as an intermediate in the production of benzoic acid, benzaldehyde, explosives, dyes and many other organic compounds(3) may also result in its release to the environment through various waste streams(SRC).

[(1) Graedel TE; Chemical Compounds in the Atmosphere. NY, NY: Academic Press p. 108 (1978) (2) Walker P; Air Pollution Assessment of Toluene. TR-7215 Mitre Corp, McLean VA, pp. 1-22, 46-92 (1976) (3) Budvari S; Merck Index, 12th ed, Whitehouse Station, NJ Merck & Co. p 1626 (1996)]**PEER REVIEWED**

TOLUENE

CASRN: 108-88-3

For other data, click on the Table of Contents

Environmental Fate:

TERRESTRIAL FATE: Based on a classification scheme(1), Koc values of 37-178 measured in soil(2,3), indicates that **toluene** is expected to have high to moderate mobility in soil(SRC). Volatilization of **toluene** from moist soil surfaces is expected to be an important fate process(SRC) given a Henry's Law constant of 6.64X10-3 atm-cu m/mole(4). **Toluene** may volatilize from dry soil surfaces based on a vapor pressure of 28.4 mm Hg at 25 deg C(5). Complete biodegradation of **toluene** was observed in lab microcosm tests during a 40 hour incubation period using soils previously exposed to **toluene**(6). The biodegradation half-life in various soils was reported as several hours to 71 days(7).

[(1) Swann RL et al; Res Rev 85: 17-28 (1983) (2) Wilson JT et al; J Environ Qual 10: 501-6 (1981) (3) Nathwani JS, Phillips CR; Chemosphere 6: 157-62 (1977) (4) Mackay D et al; Environ Sci Technol 13: 333-36 (1979) (5) Daubert TE, Danner RP; Physical and Thermodynamic Properties of Pure Chemicals Data Compilation Washington, DC: Taylor and Francis (1989) (6) Allen-King RM et al; Environ Toxicol Chem 13: 693-705 (1994) (7) Aronson D et al; Aerobic biodegradation of organic chemicals in environmental media: a summary of field and laboratory studies. USEPA (1999)]**PEER REVIEWED**

AQUATIC FATE: Based on a classification scheme(1), a Koc value of 166 measured in lake sediment(2) indicates that **toluene** is not expected to adsorb to suspended solids and sediment(SRC). Volatilization from water surfaces is expected(3) based upon a Henry's Law constant of 6.64X10-3 atm-cu m/mole(4). Using this Henry's Law constant and an estimation method(3), volatilization half-lives for a model river and model lake are 1 hour and 4 days, respectively(SRC). According to a classification scheme(5), BCF values of 13(6) and 90(7) measured in fish, suggest bioconcentration in aquatic organisms is low to moderate. The half-life of **toluene** in aerobic and anaerobic water was reported as 4 and 56 days, respectively(8).

[(1) Swann RL et al; Res Rev 85: 17-28 (1983) (2) Kan AT et al; Environ Sci Technol 32: 892-902 (1998) (3) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington, DC: Amer Chem Soc pp. 4-9, 15-1 to 15-29 (1990) (4) Mackay D et al; Environ Sci Technol 13: 333-36 (1979) (5) Franke C et al; Chemosphere 29: 1501- 14 (1994) (6) Ogata M, Miyake Y; Water Res 12: 1041-4 (1978) (7) Freitag D et al; Chemsophere 14: 1589-1616 (1985) (8) Capel PD, Larson SL; Chemosphere 30: 1097-1107 (1995)]**PEER REVIEWED**

ATMOSPHERIC FATE: According to a model of gas/particle partitioning of semivolatile organic compounds in the atmosphere(1), **toluene**, which has a vapor pressure of 28.4 mm Hg at 25 deg C(2), is expected to exist solely as a vapor in the ambient atmosphere. Vapor-phase **toluene** is degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals, nitrate radicals and ozone molecules(SRC). The half-life for the reaction with hydroxyl radicals is estimated to be 3 days(SRC), calculated from its rate constant of 5.96X10-12 cu cm/molecule-sec at 25 deg C(3). The half-life for the nighttime reaction with nitrate radicals is estimated as 491 days(SRC) calculated from its rate constant of

6.8X10-17 cu cm/molecule-sec at 25 deg C(3). The half-life for the reaction with ozone is estimated as 27,950 days(SRC) calculated from its rate constant of 4.1X10-22 cu cm/molecule-sec at 25 deg C(3). [(1) Bidleman TF; Environ Sci Technol 22: 361-367 (1988) (2) Daubert TE, Danner RP; Physical and Thermodynamic Properties of Pure Chemicals Data Compilation Washington, DC: Taylor and Francis (1989)(3) Atkinson R; J Phys Chem Ref Data Monograph 2 (1994)]**PEER REVIEWED**

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Environmental Biodegradation:

Toluene is readily degradable in a variety of standard biodegradability tests using sewage seed or sludge inoculums(1-7). Degradation has been observed in several die-away tests using seawater or estuarine water(9-12). The degradation rate is much faster in systems which have been contaminated by oil(9,10). Complete degradation has been observed in 4 days and 22 days in a marine mesocosm with summer and spring conditions, respectively(12), and 10 days in a 1% gas oil mixture in a North Sea coast water inoculum(8). A 90 day half-life in uncontaminated estuarine water was reduced to 30 days in oil-polluted water(10). The half-life in water collected near Port Valdez, Alaska was 12 days(9). 1.5 mM and 3 mM Ring-labeled **toluene** added to a methanogenic inoculum originally enriched from sewage sludge and incubated at 35 deg C for 60 days resulted in 3.6 and 4.5% 14-C final activity respectively(13).
[(1) Tabak HH et al; J Water Pollut Control Fed 53: 1503-8 (1981) (2) Davis EM et al; Water Res 15: 1125-7 (1981) (3) Bridie AL et al; Water Res 13: 627-30 (1979) (4) Kawasaki M; Ecotox Environ Safety 4: 444-54 (1980) (5) Malaney GW, McKinney RE; Water Sewage Works 113: 302-9 (1966) (6) Price KS et al; J Water Pollut Control Fed 46: 63-77 (1974) (7) Matsui S et al; Prog Water Technol 7: 645-59 (1975) (8) Van der Linden AC; Dev Biodegrad Hydrocarbons 1: 165-200 (1978) (9) Button DK et al; Appl Environ Microbiol 42: 708-19 (1981) (10) Lee RF; 1977 Oil Spill Conf Amer Petrol Inst p 611-6 (1977) (11) Reichardt PB et al; Environ Sci Technol 15: 75-9 (1981) (12) Wakeham SG et al; Environ Sci Technol 17: 611-7 (1983) (13) Grbic-Galic D, Vogel TM; Appl Environ Microbiol 53: 254-60 (1987)]**PEER REVIEWED**

Toluene completely degraded in groundwater in 8 days including a lag of 3-4 days while microbial populations became acclimated(1). Other investigators found that only 1-2% of **toluene** degraded in the subsurface environment(2) and >90% degraded in 4 weeks in soil cores at various depths both above and below the water table(3,5). Microbial attack proceeds via immediate hydroxylation of the benzene ring followed by ring-cleavage or oxidation of the side chain followed by hydroxylation and ring-cleavage(4).
[(1) Kappeler T, Wuhrmann K; Water Res 12: 327-33 (1978) (2) Wilson JT et al; Devel Indust Microbiol 24: 225-33 (1983) (3) McNabb JF et al; 81st Ann Mtg Amer Soc Microbiology p.213 (1981) (4) Fewson CA; FEMS Symp 12 (Microb Deg Xenobiotics Recalcitrant Cmpds): 141-79 (1981) (5) Wilson JT et al; Ground Water 21: 134-42 (1983)]**PEER REVIEWED**

Complete biodegradation of **toluene** was observed in lab microcosm tests during a 40 hour incubation period using soils previously exposed to **toluene**(1). **Toluene** was rapidly degraded in soil column experiments using acclimated soil at a rate of 8-35 mg/kg-day, and the rate followed zero-order kinetics(2). First-order degradation rate constants of 0.0005 to 0.0063 day-1 were measured for **toluene** in a gasoline-contaminated aquifer zone(3). These rate constants correspond to half-lives of 100-1,386 days(3). A first-order biodegradation rate constant of 0.045 day-1 was reported for **toluene** in an anaerobic petroleum contaminated aquifer, corresponding to a biodegradation half-life of 15 days(4). **Toluene** was rapidly biodegraded by indigenous mixed cultures in sandy aquifer material and pure

cultures isolated from the aquifer(5). The zero-order rate constant for the aquifer material was 23 mg/l-day and had a lag period of 2 days(5). The half-life of **toluene** in aerobic and anaerobic water was reported as 4 and 56 days, respectively(6). The biodegradation half-life in various soils was reported as several hours to 71 days(7).
[(1) Allen-King RM et al; Environ Toxicol Chem 13: 693-705 (1994) (2) Allen-King RM et al; J Environ Qual 25: 287-95 (1996) (3) Borden RC et al; Water Resour Res 33: 1105-15 (1997) (4) Borden RC et al; Anaerobic Biodegradation of BTEX in Aquifer Material USEPA/600/S-97/003. National Risk Management Laboratory, Ada, OK. pp. 9 (1997) (5) Alvarez PJJ, Vogel TM; Appl Environ Microbiol 57: 2981-85 (1991) (6) Capel PD, Larson SL; Chemosphere 30: 1097-1107 (1995) (7) Aronson D et al; Aerobic biodegradation of organic chemicals in environmental media: a summary of field and laboratory studies. USEPA (1999)]**PEER REVIEWED**

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Environmental Abiotic Degradation:

The rate constant for the vapor-phase reaction of **toluene** with photochemically-produced hydroxyl radicals has been measured as 5.96X10-12 cu cm/molecule-sec at 25 deg C(1). This corresponds to an atmospheric half-life of about 3 days at an atmospheric concentration of 5X10+5 hydroxyl radicals per cu cm(1). The rate constant for the vapor-phase reaction of **toluene** with nitrate radicals has been measured as 6.8X10-17 cu cm/molecule-sec at 25 deg C(1). This corresponds to an atmospheric half-life of about 491 days at an atmospheric concentration of 2.4X10+8 nitrate radicals per cu cm(2). The rate constant for the vapor-phase reaction of **toluene** with ozone has been measured as 4.1X10-22 cu cm/molecule-sec at 25 deg C(1). This corresponds to an atmospheric half-life of about 27,950 days at an atmospheric concentration of 7X10+11 ozone molecules per cu cm(3). **Toluene** is not expected to undergo hydrolysis in the environment due to the lack of hydrolyzable functional groups(4) nor to directly photolyze due to the lack of absorption in the environmental UV spectrum.
[(1) Atkinson R; J Phys Chem Ref Data Monograph 2 (1994) (2) Atkinson R et al; Atmos Environ 24: 2647-54 (1990) (3) Atkinson R, Carter WPL; Chem Rev 84: 437-70 (1984) (4) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington, DC: Amer Chem Soc pp. 7-4, 7-5 (1990)]**PEER REVIEWED**

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Environmental Bioconcentration:

The BCF of **toluene** in eels was reported as 13(1) and the BCF in golden ide was reported as 90(2). According to a classification scheme(3), this BCF data suggests bioconcentration in aquatic organisms is low to moderate.

[(1) Ogata M, Miyake Y; Water Res 12: 1041-4 (1978) (2) Freitag D et al; Chemosphere 14: 1589-1616 (1985) (3) Franke C et al; Chemosphere 29: 1501-14 (1994)]**PEER REVIEWED**

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Soil Adsorption/Mobility:

In association with clay minerals, **toluene**'s adsorption is inversely proportional to the pH of the soil. Approximately 40-70% of **toluene** applied to the surface of sandy soils is volatilized.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47 90 (1989)]**PEER REVIEWED**

The Koc of **toluene** was reported as 178 in a sandy soil(1) and as 37 (Wendover silty loam), 160 (Grimsby silt loam), 160 (Vaudreil sandy loam) and 46 (sandy soil)(2). The Koc of **toluene** in lake sediment was measured as 166(3). According to a classification scheme(4), this Koc data suggests that **toluene** is expected to have high to moderate mobility in soil.
[(1) Wilson JT et al; J Environ Qual 10: 501-6 (1981) (2) Nathwani JS, Phillips CR; Chemosphere 6: 157-62 (1977) (3) Kan AT et al; Environ Sci Technol 32: 892-902 (1998) (4) Swann RL et al; Res Rev 85: 17-28 (1983)]**PEER REVIEWED**

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Volatilization from Water/Soil:

The Henry's Law constant for **toluene** is 6.64X10-3 atm-cu m/mole(1). This Henry's Law constant indicates that **toluene** is expected to volatilize rapidly from water surfaces(2). Based on this Henry's Law constant, the volatilization half-life from a model river (1 m deep, flowing 1 m/sec, wind velocity of 3 m/sec)(2) is estimated as 1 hour(SRC). The volatilization half-life from a model lake (1 m deep, flowing 0.05 m/sec, wind velocity of 0.5 m/sec)(2) is estimated as 4 days(SRC). **Toluene**'s Henry's Law constant(1) indicates that volatilization from moist soil surfaces may occur(SRC). **Toluene** may volatilize from dry soil surfaces based upon a vapor pressure of 28.4 mm Hg at 25 deg C(3).
[(1) Mackay D et al; Environ Sci Technol 13: 333-36 (1979) (2) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington, DC: Amer Chem Soc pp. 15-1 to 15-29 (1990) (3) Daubert TE, Danner RP; Physical and Thermodynamic Properties of Pure Chemicals Data Compilation Washington, DC: Taylor and Francis (1989)]**PEER REVIEWED**

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Environmental Water Concentrations:

Toluene is detected in 28% of National Priority List (NPL) sites in groundwater. Average concentration: 5.18 ppm; Maximum concentration: 1100 ppm. /From table/

[Sullivan, J.B. Jr., G.R. Krieger (eds.). Hazardous Materials Toxicology-Clinical Principles of Environmental Health. Baltimore, MD: Williams and Wilkins, 1992. 304]**PEER REVIEWED**

GROUNDWATER: **Toluene** was detected in groundwater near contaminated wells from gasoline storage tanks at concns of 0.55-6400 ppb(1,2) and groundwater underlying 2 rapid infiltration sites at 0.2 ppb(3). Groundwater under a gasification site 15 months after gasification contained **toluene** at 170-740 ppb(4). In a cluster well study under an old industrial site, mean levels of **toluene** in bedrock wells were 90 ppb while shallow and deep glacial wells were 10 ppb(5). **Toluene** was detected in 1.3% of the samples in the US Ground Water Supply Survey, 1982, at a max concn of 2.9 ppb and a median concn of 0.8 ppb(6).

[(1) Burmaster DE; Environ 24: 6-13, 33-6 (1982) (2) Tester DJ, Harker RJ; Water Pollut Control 80: 614-31 (1981) (3) Hutchins SR et al; Environ Toxicol Chem 2: 195-216 (1983) (4) Stuermer DH et al; Environ Sci Technol 16: 582-7 (1982) (5) Rich CA; Stud Environ Sci 17(Qual Groundwater): 309-14 (1981) (6) Coturvo JA; Sci Total Environ 47: 7-26 (1985)]**PEER REVIEWED**

DRINKING WATER: **Toluene** was detected in 33% of the samples from 30 Canadian treatment facilities at an avg concn of 2 ppb (14 ppb max) in summer months and in 53% of the samples at an avg concn of <1 ppb (13 ppb max), during winter(1). **Toluene** was detected at concns of 0-2 ppb in drinking water of cities supplied by the Great Lakes(2). **Toluene** was detected in 14% of the samples of drinking water in the US at concns of less than 1 part per trillion(3). In a federal survey of finished drinking water from groundwater sources **toluene** was detected in less than 5% of the samples(4). **Toluene** was detected in 3 New Orleans area water supplies at 0-10 ppb(5). **Toluene** was identified, not quantified, in 60% of drinking water tested in the National Organics Reconnaissance Survey(6). The max concn of **toluene** in tapwater derived from bank-filtered Rhine River water was 1 ppb(7). **Toluene** was detected in 3 contaminated drinking water wells in New Jersey at 55, 260, 6400 ppb whereas the highest concn in drinking water from surface water sources was 6.1 ppb(8). Drinking water supplied from groundwater in England 210 m from a gasoline storage tank contained 0.15 ppb of **toluene**(9). In a 5-city survey in which the water supplies came from different types of sources with various sources of pollution, 2 contained **toluene**, one 0.1 ppb and the other 0.7 ppb(10). **Toluene** was detected in 20 of 182 bottled water samples at an avg concn of 6.92 ug/kg and a range of 0.5-63 ug/kg(11).

[(1) Otson R et al; J Assoc Off Analyt Chem 65: 1370-4 (1982) (2) Williams DT et al; Chemosphere 11: 263-76 (1982) (3) NAS; The Alkyl Benzene USEPA Contract No. 68-02-4655 (1980) (4) Dyksen JE, Hess AF III: J Amer Water Works Assoc 74: 394-403 (1982) (5) Keith LH et al; pp. 329-73 in Identification and analysis of organic pollutants in Water, Keith LH, ed, Ann Arbor Sci Publ (1976) (6) Bedding ND et al;

Sci Total Environ 25: 143-67 (1982) (7) Piet GJ, Morra CF; pp. 31-42 in Artificial Groundwater Recharge (Water Res Eng Ser) Huisman L, Olsthorn TN, eds, Pitman Publ (1983) (8) Burmaster DE; Environ 24: 6-13, 33-6 (1982) (9) Tester DJ, Harker RJ; Water Pollut Control 80: 614-31 (1981) (10) Coleman WE et al; pp. 305-27 in Analysis and identification of organic substances in water. Keith L, ed, Ann Arbor, MI: Ann Arbor Sci (1976) (11) Page RD et al; J AOAC Int 76: 26-31 (1993)]**PEER REVIEWED**

SURFACE WATER: **Toluene** was detected in 31 of 204 sites at concns of 1-5 ppb in 14 heavily industrialized river basins in the US(1). **Toluene** was identified, not quantified, in various rivers(2-5). **Toluene** was detected in the Gulf of Mexico at 3-376 parts per trillion(6,7) and the Vineland Sound, MA at 10-54 parts per trillion(8). **Toluene** was detected in the Elbe River, Germany at concns of 30-243 ng/l(9).
[(1) Ewing BB et al; Monitoring to detect previously unrecognized pollutants in surface waters USEPA 560/6-77-015 (appendix USEPA 560/6-77-015a) (1977) (2) Sheldon LS, Hites RA; Environ Sci Technol 12: 1188-94 (1978) (3) Goodley PC, Gordon M; KY Acad Sci 37: 11-5 (1976) (4) Zuercher F, Giger W; Vom Wasser 47: 37-55 (1976) (5) Zou H et al; Wat Res 30: 2003-2008 (1996) (6) Sauer TC Jr; Org Geochem 3: 91-101 (1981) (7) Sauer TC Jr et al; Mar Chem 7: 1-16 (1978) (8) Gschwend PM et al; Environ Sci Technol 16: 31-8 (1982) (9) Gotz R et al; Chemosphere 36: 2103-18 (1998)]**PEER REVIEWED**

RAIN WATER: **Toluene** was detected in rain in west Los Angeles at 76 parts per trillion(1). **Toluene** was detected in 71.4% of the rain samples from 7 rain events in Portland, OR, Feb-Apr 1984, at concns of 40-220 parts per trillion(2).
[(1) Kawamura K, Kaplan IR; Environ Sci Technol 17: 497-501 (1983) (2) Ligocki MP et al; Atmos Environ 19: 1609-17 (1985)]**PEER REVIEWED**

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Effluent Concentrations:

Industries in which the mean effluent levels exceed 1000 ppb are: auto and other laundries, iron and steel manufacturing, gum and wood chemicals, pharmaceuticals, organic chemicals/plastics manufacturing, paint and ink formulation. The highest mean value is 52 ppm for pharmaceuticals and the highest maximum values are 230 and 260 ppm for pharmaceuticals and organic chemicals/plastics manufacturing(1). **Toluene** was detected in a plume from General Motors Paint Plant, Janesville, WI at 156 ppb(2). Auto exhaust contained **toluene** at concns of 196-718 mg/cu m(3).
[(1) USEPA; Treatability Manual p. I.9.10-1 to I.9.10-5 USEPA 600/2-82-001a (1981) (2) Sexton K, Westberg H; Environ Sci Technol 14: 329-32 (1980) (3) Tsani-Bazaca E et al; Environ Technol Lett 2: 303-16 (1981)]**PEER REVIEWED**

Toluene was detected in landfill gas emissions at concns of 20,400 ppb, 34,907 ppb and 76,700 ppb(1). **Toluene** was detected in the gas emissions of 7 waste disposal sites in the UK at concns of 10-287 mg/cu m(2). **Toluene** was identified, not quantified, in the exhaust of a moped(3) and 4-stroke lawn mower(4). **Toluene** was detected in car exhaust under normal operating conditions at concns of 3.31-4.52 ppm and an avg of 3.83 ppm(5). The mean emission rate of **toluene** is 89-453 mg/km, with the lowest emission rates occurring at higher driving speeds(5). **Toluene** was detected in the effluent of a hazardous waste incinerator in Germany at a concn of 34 ug/cu m(6).
[(1) Brosseau J, Heitz M; Atmos Environ 28: 285-93 (1994) (2) Allen MR et al; Environ Sci Technol 31: 1054-61 (1997) (3) Ostermark U, Petersson G: Chemosphere 27: 1719-28 (1993) (4) Gabele P; J air Waste Manage Assoc 47: 945-52 (1997) (5) Baily JC et al; Atmos Environ 24A: 43-52 (1990) (6) Jay K, Stiegltz L; Chemosphere 30: 1249-60 (1995)]**PEER REVIEWED**

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Sediment/Soil Concentrations:

SEDIMENT: **Toluene** was identified, not quantified in sediment from rivers near industrial facilities in the US(1,2). USEPA STORET DATABASE: **Toluene** was detected in 67 of 397 sediment samples at a median concn of 5.0 ppb dry weight(3). **Toluene** was detected in 33% of the sediment samples from Lake Pontchartrain, LA at an avg concn of 0.7 ppb wet weight(4). **Toluene** was detected at concns of less than 0.1 ng/g to 1.2 ng/g in sediment from rivers near Niigata, Japan(5). **Toluene** was detected in sediment of the Passaic River, NJ at concns of 3-250 ug/kg(6).

[(1) Goodley PC, Gordon M; KY Acad Sci 37: 11-5 (1976) (2) Steinheimer TR et al; Anal Chim Acta 129: 57-67 (1981) (3) Staples CA et al; Environ Toxicol Chem 4: 131-42 (1985) (4) Ferrario JB et al; Bull Environ Contam Toxicol 34: 246-55 (1985) (5) Kawata K et al; Bull Environ Contam Toxicol 58: 893-900 (1997) (6) Iannuzzi TJ et al; Chemosphere 34: 213-31 (1997)]**PEER REVIEWED**

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Atmospheric Concentrations:

URBAN/SUBURBAN: In a survey of 3,195 samples obtained from urban areas in the US, **toluene** was detected at concns of 0-85 ppb (11 ppb median)(1). Average **toluene** concns in US cities range from 0.8-37 ppb with max values ranging from 6.5-1,110 ppb(2-9). Daily variations in concentrations and ratios of **toluene** to benzene indicate that auto traffic is the most common source of atmospheric **toluene**(10,11,12). **Toluene** was detected in Middelsbrough, UK and London, UK at 1.55 and 7.475 ppb, respectively(13). The avg concn of **toluene** inside buses and cars in Taipei, Taiwan was reported as 367 and 599 ug/cu m(14). **Toluene** was detected in various streets in Europe at concns of 87-127 ug/cu m(15). The concn of **toluene** inside automobiles in Paris, France was 178-258 ug/cu m(16).
[(1) Brodzinsky R, Singh HB; Volatile Organics in the Atmosphere: An Assessment of Available Data. p 126-7 SRI contract 68-02-3459 (1982) (2) Singh HB et al; Atmospheric measurements of Selected Hazardous Organic Chemicals USEPA 600/53-81-032 (1981) (3) Altshuller AP et al; Environ Sci Technol 5: 1009-16 (1971) (4) Singh HB et al; Atmos Environ 15: 601-12 (1981) (5) Arnts RR, Meeks SA; Biogenic hydrocarbon contribution to the ambient air of selected areas 128 USEPA 600/3-80-023 (1980) (6) Bozzelli JW et al; Analysis of selected toxic and carcinogenic substances in ambient air in New Jersey, NJ Dept Environ Protect (1980) (7) Lonneman WA et al; Hydrocarbons in Houston air. USEPA 600/3-79-018 pp. 44 (1979) (8) Lioy PJ et al; J Water Pollut Control Fed 33: 649-57 (1983) (9) Pilar S, Graydon WF; Environ Sci Technol 7: 628-71 (1973) (10) Termonia M; Comm Eur Comm EUR 7624 pp. 356-61 (1982) (11) Sexton K, Westberg H; Environ Sci Technol 14: 329-32 (1980) (12) Tsani-Bazaca E et al; Chemosphere 11: 11-23 (1982) (13) Derwent RG; pp. 1-15 in Volatile Organic Compounds in the Atmosphere. Hester RE, Harrison RM, Iss Environ Sci Technol No 4, the Royal Society of Chemistry, Cambridge, UK (1995) (14) Chan CC et al; Atmos Environ 28: 2351-59 (1994) (15) Coursimault A et al; Sci Total Environ 169: 17-23 (1995) (16) Dor F et al; J Air Waste Manage Assoc 45: 103-110 (1995)]**PEER REVIEWED**

INDOOR AIR: **Toluene** was detected at mean concns of 4.8 ug/cu m in telephone communications offices, 10.1 ug/cu m in data center offices and 5.7 ug/cu m in administrative offices in the US(1). **Toluene** was detected in the volatile emissions of newly installed carpet cushions at an emission rate of 4-79 ug/sq m-hr during the first 6 hours after installation(2). **Toluene** was detected in hairdresser salons in Norway at concns of 0.04-0.11 mg/cu m(3).
[(1) Shields HC et al; Indoor air 6: 2-17 (1996) (2) Schaeffer VH et al; J Air Waste Manage Assoc 46: 813-20 (1996) (3) Hollund BE, Moen BE; Ann Occup Hyg 42: 277-81 (1998)]**PEER REVIEWED**

RURAL/REMOTE: **Toluene** was detected in the atmosphere of 115 remote samples taken in the US at concns of 0.057-30 ppb, (0.66 ppb median)(1). **Toluene** was identified, not quantified, in a forest in

Germany(2). **Toluene** was detected in Langenbrugge, Germany and West Beckham, UK at concns of 0.441 and 0.999 ppb, respectively(3). **Toluene** was detected at a concn of 0.04 ppb in Izana, Canaries(3) [(1) Brodzinsky R, Singh HB; Volatile Organics in the Atmosphere: An Assessment of Available Data. pp. 126-7 SRI contract 68-02-3459 (1982) (2) Helmig D et al; Chemosphere 19: 1399-1412 (1989) (3) Derwent RG; pp. 1-15 in Volatile Organic Compounds in the Atmosphere, Hester RE, Harrison RM. Iss Environ Sci Technol No 4, the Royal Society of Chemistry, Cambridge, UK (1995)]**PEER REVIEWED**

SOURCE DOMINATED: In a survey of 188 source dominated samples from the US, **toluene** was detected at concns of 0.037-5,500 ppb (4.6 ppb median)(1). **Toluene** was detected in the air of the Lipari and BFI landfills in NJ at 0.40 and 310 ppb(2). **Toluene** was detected at concns of 14-22 ppb 4 miles downwind from a General Motors paint plant(3). The avg concn of **toluene** around gasoline pumps during fueling was in the range of 0.14-1.2 mg/cu m and the fenceline concns at the filling stations were in the range of 0.005-0.02 ppm(4). **Toluene** was detected in the Fort McHenry Tunnel, MD at concns of 79-90 ppb(5).
[(1) Brodzinsky R, Singh HB; Volatile Organics in the Atmosphere: An Assessment of Available Data. pp. 126-7 SRI contract 68-02-3459 (1982) (2) Bozzelli JW et al; Analysis of selected toxic and carcinogenic substances in ambient air in New Jersey, NJ Dept Environ Protect (1980) (3) Tsani-Bazaca E et al; Chemosphere 11: 11-23 (1982) (4) American Petroleum Inst; Gasoline Vapor Exposure Assessment at Service Stations. American Petroleum Inst Washington, DC: API Publ 4553 (1993) (5) Zielinska B et al; Atmos Environ 12: 2269-86 (1996)]**PEER REVIEWED**

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Food Survey Values:

Toluene was identified, not quantified, in baked potatoes(1), mountain cheese(2), fried bacon(3), fried chicken(4), peanut oil(5) and raw beef(6).

[(1) Coleman EC et al; J Agric Food Chem 29: 42-8 (1981) (2) Dumont JP, Adda J; J Agric Food Chem 26: 364-7 (1978) (3) Ho CT et al; J Agric Food Chem 31: 336-42 (1983) (4) Tang JT et al; J Agric Food Chem 31: 1287-92 (1983) (5) Chung TY et al; J Agric Food Chem 41: 1467-70 (1993) (6) King MF et al; J Agric Food Chem 41: 1974-81 (1993)]**PEER REVIEWED**

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Plant Concentrations:

Toluene was identified, not quantified, in the Korean Chamachwi plant(1).

[(1) Chung TY et al; J Agric Food Chem 41: 1693-97 (1993)]**PEER REVIEWED**

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Fish/Seafood Concentrations:

Flesh of fish from petroleum contaminated harbor in Japan contained **toluene** at 5 ppm(1). **Toluene** was detected in oysters from Lake Pontchartrain, LA at an avg concn of 3.4 ppb and clams at concns of 18 and 11 ppb(2). **Toluene** was identified, not quantified, in boiled shrimp and crab(3).

[(1) USEPA; Ambient Water Quality Criteria for Toluene. pp. C-1 to C-7 (1980) (2) Ferrario JB et al; Bull Environ Contam Toxicol 34: 246-55 (1985) (3) Misharina TA, Golovnya RV; J High Resol Chromat 15: 332-34 (1992)]**PEER REVIEWED**

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Milk Concentrations:

Toluene was identified, not quantified, in 8 samples of mothers' milk from 4 urban areas(1).

[(1) Pellizzari ED et al; Bull Environ Contam Toxicol 28: 322-8 (1982)]**PEER REVIEWED**

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Other Environmental Concentrations:

Light oil from coal 12-20% **toluene**; crude oil 1.2-2.4% auto fuel 8-12%(1).
[(1) Walker P; Air Pollution Assessment of Toluene. p. 1-22, 46-92 MTR-7215 Mitre Corp, McLean VA (1976)]**PEER REVIEWED**

Evaporation from gasoline tank: 0.3 - 0.9 vol % of total evaporated hydrocarbons; evaporation from carburetor: 0.5 - 2.4 vol % of total evaporated hydrocarbons.
[Verschueren, K. Handbook of Environmental Data on Organic Chemicals. 3rd ed. New York, NY: Van Nostrand Reinhold Co., 1996. 1723]**PEER REVIEWED**

In exhaust of gasoline engines: 3-8 vol% of total exhaust hydrocarbons; in exhaust of diesel engine: 3% of emitted hydrocarbons; in exhaust of rotary gasoline engine: 16% of emitted hydrocarbons; in exhaust of gasoline engine: 0.1-7.0 ppm (partly crotonaldehyde); in 4 municipal landfill gases in S. Finland (1989-1990): avg 0.23-137, max 143 mg/cu m.
[Verschueren, K. Handbook of Environmental Data on Organic Chemicals. 3rd ed. New York, NY: Van Nostrand Reinhold Co., 1996. 1723]**PEER REVIEWED**

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For other data, click on the Table of Contents

Environmental Standards & Regulations:

FIFRA Requirements:

Toluene is exempted from the requirement of a tolerance when used as a solvent or cosolvent in accordance with good agricultural practice as inert (or occasionally active) ingredients in pesticide formulations applied to growing crops only.
[40 CFR 180.1001(d) (7/1/99)]**PEER REVIEWED**

TSCA Requirements:

Pursuant to section 8(d) of TSCA, EPA promulgated a model Health and Safety Data Reporting Rule. The section 8(d) model rule requires manufacturers, importers, and processors of listed chemical substances and mixtures to submit to EPA copies and lists of unpublished health and safety studies. **Toluene** is included on this list.
[40 CFR 716.120 (7/1/99)]**PEER REVIEWED**

CERCLA Reportable Quantities:

Persons in charge of vessels or facilities are required to notify the National Response Center (NRC) immediately, when there is a release of this designated hazardous substance, in an amount equal to or greater than its reportable quantity of 1000 lb or 454 kg. The toll free number of the NRC is (800) 424-8802; In the Washington D.C. metropolitan area (202) 426-2675. The rule for determining when notification is required is stated in 40 CFR 302.4 (section IV. D.3.b).
[40 CFR 302.4 (7/1/99)]**PEER REVIEWED**

RCRA Requirements:

U220; As stipulated in 40 CFR 261.33, when **toluene**, as a commercial chemical product or manufacturing chemical intermediate or an off-specification commercial chemical product or a manufacturing chemical intermediate, becomes a waste, it must be managed according to Federal and/or State hazardous waste regulations. Also defined as a hazardous waste is any residue, contaminated soil, water, or other debris resulting from the cleanup of a spill, into water or on dry land, of this waste. Generators of small quantities of this waste may qualify for partial exclusion from hazardous waste regulations (40 CFR 261.5).
[40 CFR 261.33 (7/1/99)]**PEER REVIEWED**

F005; When **toluene** is a spent solvent, it is classified as a hazardous waste from a nonspecific source (F005), as stated in 40 CFR 261.31, and must be managed according to State and/or Federal hazardous waste regulations.
[40 CFR 261.31 (7/1/99)]**PEER REVIEWED**

Atmospheric Standards:

This action promulgates standards of performance for equipment leaks of Volatile Organic Compounds

(VOC) in the Synthetic Organic Chemical Manufacturing Industry (SOCMI). The intended effect of these standards is to require all newly constructed, modified, and reconstructed SOCMI process units to use the best demonstrated system of continuous emission reduction for equipment leaks of VOC, considering costs, non air quality health and environmental impact and energy requirements. **Toluene** is produced, as an intermediate or a final product, by process units covered under this subpart.
[40 CFR 60.489 (7/1/99)]**PEER REVIEWED**

Listed as a hazardous air pollutant (HAP) generally known or suspected to cause serious health problems. The Clean Air Act, as amended in 1990, directs EPA to set standards requiring major sources to sharply reduce routine emissions of toxic pollutants. EPA is required to establish and phase in specific performance based standards for all air emission sources that emit one or more of the listed pollutants. **Toluene** is included on this list.
[Clean Air Act as amended in 1990, Sect. 112 (b) (1) Public Law 101-549 Nov. 15, 1990]**PEER REVIEWED**

Clean Water Act Requirements:

Toxic pollutant designated pursuant to section 307(a)(1) of the Federal Water Pollution Control Act and is subject to effluent limitations.
[40 CFR 401.15 (7/1/99)] **QC REVIEWED**

Toluene is designated as a hazardous substance under section 311(b)(2)(A) of the Federal Water Pollution Control Act and further regulated by the Clean Water Act Amendments of 1977 and 1978. These regulations apply to discharges of this substance. This designation includes any isomers and hydrates, as well as any solutions and mixtures containing this substance.
[40 CFR 116.4 (7/1/99)] **QC REVIEWED**

For the protection of human health from the toxic properties of **toluene** ... the ambient water criterion is determined to be 14.3 mg/l.
[USEPA; Quality Criteria for Water 1986: Toluene (1986) EPA 440/5-86-001] **QC REVIEWED**

The maximum contaminant level (MCL) set forth by the National Revised Primary Drinking Water Regulations for the organic contaminant **toluene** in community and non-transient, non-community water systems is 1 mg/l.
[40 CFR 141.61 (7/1/99)] **QC REVIEWED**

Federal Drinking Water Standards:

EPA 1000 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

Federal Drinking Water Guidelines:

EPA 1000 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water

Standards and Guidelines (11/93)] **QC REVIEWED**

State Drinking Water Standards:

(CA) CALIFORNIA 150 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

(WI) WISCONSIN 1000 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

State Drinking Water Guidelines:

(AZ) ARIZONA 2000 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

(CT) CONNECTICUT 1000 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

(FL) FLORIDA 40 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

(ME) MAINE 1400 ug/l
[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

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[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

(WI) WISCONSIN 343 ug/l
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FDA Requirements:

Toluene is an indirect food additive for use only as a component of adhesives.
[21 CFR 175.105 (4/1/99)]**PEER REVIEWED**

Allowable Tolerances:

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For other data, click on the Table of Contents

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[40 CFR 716.120 (7/1/99)]**PEER REVIEWED**

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[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

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[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

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[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)] **QC REVIEWED**

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[21 CFR 175.105 (4/1/99)]**PEER REVIEWED**

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[40 CFR 180.1001(d) (7/1/99)]**PEER REVIEWED**

TOLUENE

CASRN: 108-88-3

For other data, click on the Table of Contents

Chemical/Physical Properties:

Molecular Formula:

C7-H8
PEER REVIEWED

Molecular Weight:

92.14
[Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 79th ed. Boca Raton, FL: CRC Press Inc., 1998-1999.,p. 3-55]**PEER REVIEWED**

Color/Form:

Colorless liquid.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 310]**PEER REVIEWED**

Odor:

Sweet, pungent, benezene-like odor.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 310]**PEER REVIEWED**

Boiling Point:

110.6 deg C
[Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 79th ed. Boca Raton, FL: CRC Press Inc., 1998-1999.,p. 3-55]**PEER REVIEWED**

Melting Point:

-94.9 deg C
[Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 79th ed. Boca Raton, FL: CRC Press Inc., 1998-1999.,p. 3-55]**PEER REVIEWED**

Corrosivity:

Noncorrosive liquid.
[USEPA; Ambient Water Quality Doc: Toluene p.A-1 (1980) EPA 440/5-80-075)]**PEER REVIEWED**

Critical Temperature & Pressure:

Critical temperature: 591.75 K; Critical pressure: 4.108 MPa
[Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 79th ed. Boca Raton, FL: CRC Press Inc., 1998-1999.,p. 6-54]**PEER REVIEWED**

Density/Specific Gravity:

0.8636 @ 20 deg C/4 deg C
[Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 79th ed. Boca Raton, FL: CRC Press Inc., 1998-1999.,p. 3-55]**PEER REVIEWED**

Heat of Combustion:

3910.3 KJ/mol
[Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 79th ed. Boca Raton, FL: CRC Press Inc., 1998-1999.,p. 6-111]**PEER REVIEWED**

Heat of Vaporization:

38.01 KJ/mol @ 25 deg C
[Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 79th ed. Boca Raton, FL: CRC Press Inc., 1998-1999.,p. 6-111]**PEER REVIEWED**

Octanol/Water Partition Coefficient:

log Kow= 2.73
[Hansch, C., Leo, A., D. Hoekman. Exploring QSAR - Hydrophobic, Electronic, and Steric Constants. Washington, DC: American Chemical Society., 1995. 31]**PEER REVIEWED**

Solubilities:

Miscible with alcohol, chloroform, ether, acetone, glacial acetic acid, carbon disulfide
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 1626]**PEER REVIEWED**

Soluble in ethanol, benzene, diethyl ether, acetone, chloroform, glacial acetic acid and carbon disulfide; insoluble in water.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47 79 (1989)]**PEER REVIEWED**

In water, 526 mg/l @ 25 deg C
[Sanemasa I et al; Bull Chem Soc Japan 55: 1054-62 (1982)]**PEER REVIEWED**

Spectral Properties:

SADTLER REF NUMBER: 419 (IR, PRISM); 119 (IR, GRATING); MAX ABSORPTION (ALCOHOL): 207 NM (LOG E= 3.97); 260 NM LOG E= 2.48)

[Weast, R.C. (ed.). Handbook of Chemistry and Physics. 60th ed. Boca Raton, Florida: CRC Press Inc., 1979.,p. C-518]**PEER REVIEWED**

Index of refraction: 1.4967 @ 20 deg C/D
[Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 79th ed. Boca Raton, FL: CRC Press Inc., 1998-1999.,p. 3-55]**PEER REVIEWED**

IR: 3574 (Coblentz Society Spectral Collection)
[Weast, R.C. and M.J. Astle. CRC Handbook of Data on Organic Compounds. Volumes I and II. Boca Raton, FL: CRC Press Inc. 1985.,p. V2 360]**PEER REVIEWED**

UV: 155 (Sadtler Research Laboratories Spectral Collection)
[Weast, R.C. and M.J. Astle. CRC Handbook of Data on Organic Compounds. Volumes I and II. Boca Raton, FL: CRC Press Inc. 1985.,p. V2 360]**PEER REVIEWED**

NMR: 157 (Varian Associates NMR Spectra Catalogue)
[Weast, R.C. and M.J. Astle. CRC Handbook of Data on Organic Compounds. Volumes I and II. Boca Raton, FL: CRC Press Inc. 1985.,p. V2 360]**PEER REVIEWED**

MASS: 189 (Atlas of Mass Spectral Data, John Wiley & Sons, New York)
[Weast, R.C. and M.J. Astle. CRC Handbook of Data on Organic Compounds. Volumes I and II. Boca Raton, FL: CRC Press Inc. 1985.,p. V2 360]**PEER REVIEWED**

Intense mass spectral peaks: 65 m/z, 91 m/z, 92 m/z
[Pfleger, K., H. Maurer and A. Weber. Mass Spectral and GC Data of Drugs, Poisons and their Metabolites. Parts I and II. Mass Spectra Indexes. Weinheim, FederalRepublic of Germany. 1985. 104]**PEER REVIEWED**

Surface Tension:

29.71 dyne/cm @ 10 deg C; 28.93 dyne/cm @ 20 deg C; 24.96 dyne/cm @ 50 deg C; 21.98 dyne/cm @ 75 deg C; 19.01 dyne/cm @ 100 deg C
[Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 79th ed. Boca Raton, FL: CRC Press Inc., 1998-1999.,p. 6-137]**PEER REVIEWED**

Vapor Density:

3.1 (Air=1)
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994.,p. 1304-5]**PEER REVIEWED**

Vapor Pressure:

28.4 mm Hg @ 25 deg C
[Daubert, T.E., R.P. Danner. Physical and Thermodynamic Properties of Pure Chemicals Data Compilation. Washington, D.C.: Taylor and Francis, 1989.]**PEER REVIEWED**

Viscosity:

0.778 cP @ 0 deg C; 0.560 cP @ 25 deg C; 0.424 cP @ 50 deg C; 0.333 cP @ 75 deg C; 0.270 cP @ 100 deg C
[Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 79th ed. Boca Raton, FL: CRC Press Inc., 1998-1999.,p. 6-173]**PEER REVIEWED**

Other Chemical/Physical Properties:

CONVERSION FACTORS: 1 PPM= 3.76/CU M; 1 MG/L= 226 PPM.
[Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965. 66]**PEER REVIEWED**

Ratio of Specific Heats of Vapor (Gas): 1.089; floats on water
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Partition coefficients at 37 deg C for **toluene** into blood= 15.6; into oil= 1,470.
[Sato A, Nakajima T; Scand J Work Environ Health 13: 81-93 (1987)]**PEER REVIEWED**

Henry's Law constant = 6.64X10-3 atm-cu m/mole @ 25 deg C
[Mackay D et al; Environ Sci Technol 13: 333-6 (1979)]**PEER REVIEWED**

Hydroxyl radical rate constant = 5.96X10-12 cu cm/molecule-sec @ 25 deg C
[Atkinson R; J Phys Chem Ref Data Monograph No. 2 (1994)]**PEER REVIEWED**

TOLUENE

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Molecular Formula:

C7-H8

PEER REVIEWED

TOLUENE

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TOLUENE

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Color/Form:

Colorless liquid.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 310]**PEER REVIEWED**

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Sweet, pungent, benezene-like odor.

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110.6 deg C

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CASRN: 108-88-3

For other data, click on the Table of Contents

Heat of Combustion:

3910.3 KJ/mol

[Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 79th ed. Boca Raton, FL: CRC Press Inc., 1998-1999.,p. 6-111]**PEER REVIEWED**

TOLUENE

CASRN: 108-88-3

For other data, click on the Table of Contents

Heat of Vaporization:

38.01 KJ/mol @ 25 deg C
[Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 79th ed. Boca Raton, FL: CRC Press Inc., 1998-1999.,p. 6-111]**PEER REVIEWED**

TOLUENE

CASRN: 108-88-3

For other data, click on the Table of Contents

Octanol/Water Partition Coefficient:

log Kow= 2.73

[Hansch, C., Leo, A., D. Hoekman. Exploring QSAR - Hydrophobic, Electronic, and Steric Constants. Washington, DC: American Chemical Society., 1995. 31]**PEER REVIEWED**

TOLUENE

CASRN: 108-88-3

For other data, click on the Table of Contents

Solubilities:

Miscible with alcohol, chloroform, ether, acetone, glacial acetic acid, carbon disulfide

[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 1626]**PEER REVIEWED**

Soluble in ethanol, benzene, diethyl ether, acetone, chloroform, glacial acetic acid and carbon disulfide; insoluble in water.

[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47 79 (1989)]**PEER REVIEWED**

In water, 526 mg/l @ 25 deg C

[Sanemasa I et al; Bull Chem Soc Japan 55: 1054-62 (1982)]**PEER REVIEWED**

TOLUENE

CASRN: 108-88-3

For other data, click on the Table of Contents

Spectral Properties:

SADTLER REF NUMBER: 419 (IR, PRISM); 119 (IR, GRATING); MAX ABSORPTION (ALCOHOL): 207 NM (LOG E= 3.97); 260 NM LOG E= 2.48)
[Weast, R.C. (ed.). Handbook of Chemistry and Physics. 60th ed. Boca Raton, Florida: CRC Press Inc., 1979.,p. C-518]**PEER REVIEWED**

Index of refraction: 1.4967 @ 20 deg C/D
[Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 79th ed. Boca Raton, FL: CRC Press Inc., 1998-1999.,p. 3-55]**PEER REVIEWED**

IR: 3574 (Coblentz Society Spectral Collection)
[Weast, R.C. and M.J. Astle. CRC Handbook of Data on Organic Compounds. Volumes I and II. Boca Raton, FL: CRC Press Inc. 1985.,p. V2 360]**PEER REVIEWED**

UV: 155 (Sadtler Research Laboratories Spectral Collection)
[Weast, R.C. and M.J. Astle. CRC Handbook of Data on Organic Compounds. Volumes I and II. Boca Raton, FL: CRC Press Inc. 1985.,p. V2 360]**PEER REVIEWED**

NMR: 157 (Varian Associates NMR Spectra Catalogue)
[Weast, R.C. and M.J. Astle. CRC Handbook of Data on Organic Compounds. Volumes I and II. Boca Raton, FL: CRC Press Inc. 1985.,p. V2 360]**PEER REVIEWED**

MASS: 189 (Atlas of Mass Spectral Data, John Wiley & Sons, New York)
[Weast, R.C. and M.J. Astle. CRC Handbook of Data on Organic Compounds. Volumes I and II. Boca Raton, FL: CRC Press Inc. 1985.,p. V2 360]**PEER REVIEWED**

Intense mass spectral peaks: 65 m/z, 91 m/z, 92 m/z
[Pfleger, K., H. Maurer and A. Weber. Mass Spectral and GC Data of Drugs, Poisons and their Metabolites. Parts I and II. Mass Spectra Indexes. Weinheim, FederalRepublic of Germany. 1985. 104]**PEER REVIEWED**

TOLUENE

CASRN: 108-88-3

For other data, click on the Table of Contents

Surface Tension:

29.71 dyne/cm @ 10 deg C; 28.93 dyne/cm @ 20 deg C; 24.96 dyne/cm @ 50 deg C; 21.98 dyne/cm @ 75 deg C; 19.01 dyne/cm @ 100 deg C

[Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 79th ed. Boca Raton, FL: CRC Press Inc., 1998-1999.,p. 6-137]**PEER REVIEWED**

TOLUENE

CASRN: 108-88-3

For other data, click on the Table of Contents

Vapor Density:

3.1 (Air=1)

[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994.,p. 1304-5]**PEER REVIEWED**

TOLUENE

CASRN: 108-88-3

For other data, click on the Table of Contents

Vapor Pressure:

28.4 mm Hg @ 25 deg C

[Daubert, T.E., R.P. Danner. Physical and Thermodynamic Properties of Pure Chemicals Data Compilation. Washington, D.C.: Taylor and Francis, 1989.]**PEER REVIEWED**

TOLUENE

CASRN: 108-88-3

For other data, click on the Table of Contents

Viscosity:

0.778 cP @ 0 deg C; 0.560 cP @ 25 deg C; 0.424 cP @ 50 deg C; 0.333 cP @ 75 deg C; 0.270 cP @ 100 deg C

[Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 79th ed. Boca Raton, FL: CRC Press Inc., 1998-1999.,p. 6-173]**PEER REVIEWED**

TOLUENE

CASRN: 108-88-3

For other data, click on the Table of Contents

Other Chemical/Physical Properties:

CONVERSION FACTORS: 1 PPM= 3.76/CU M; 1 MG/L= 226 PPM.
[Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965. 66]**PEER REVIEWED**

Ratio of Specific Heats of Vapor (Gas): 1.089; floats on water
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Partition coefficients at 37 deg C for **toluene** into blood= 15.6; into oil= 1,470.
[Sato A, Nakajima T; Scand J Work Environ Health 13: 81-93 (1987)]**PEER REVIEWED**

Henry's Law constant = 6.64X10-3 atm-cu m/mole @ 25 deg C
[Mackay D et al; Environ Sci Technol 13: 333-6 (1979)]**PEER REVIEWED**

Hydroxyl radical rate constant = 5.96X10-12 cu cm/molecule-sec @ 25 deg C
[Atkinson R; J Phys Chem Ref Data Monograph No. 2 (1994)]**PEER REVIEWED**

TOLUENE

CASRN: 108-88-3

For other data, click on the Table of Contents

Chemical Safety & Handling:

DOT Emergency Guidelines:

Fire or explosion: Highly flammable: Will be easily ignited by heat, sparks or flames. Vapors may form explosive mixtures with air. Vapors may travel to source of ignition and flash back. Most vapors are heavier than air. They will spread along ground and collect in low or confined areas (sewers, basements, tanks). Vapor explosion hazard indoors, outdoors or in sewers. Some may polymerize (P) explosively when heated or involved in a fire. Runoff to sewer may create fire or explosion hazard. Containers may explode when heated. Many liquids are lighter than water.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-130]**PEER REVIEWED**

Health: May cause toxic effects if inhaled or absorbed through skin. Inhalation or contact with material may irritate or burn skin and eyes. Fire will produce irritating, corrosive and/or toxic gases. Vapors may cause dizziness or suffocation. Runoff from fire control or dilution water may cause pollution.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-130]**PEER REVIEWED**

Public safety: Call Emergency Response Telephone Numbers. ... Isolate spill or leak area immediately for at least 50 to 100 meters (160 to 330 feet) in all directions. Keep unauthorized personnel away. Stay upwind. Keep out of low areas. Ventilate closed spaces before entering.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-130]**PEER REVIEWED**

Protective clothing: Wear positive pressure self-contained breathing apparatus (SCBA). Structural firefighters' protective clothing will only provide limited protection.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs

Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-130]**PEER REVIEWED**

Evacuation: Large spill: Consider initial downwind evacuation for at least 300 meters (1000 feet). Fire: If tank, rail car or tank truck is involved in a fire, isolate for 800 meters (1/2 mile) in all directions; also, consider initial evacuation for 800 meters (1/2 mile) in all directions.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-130]**PEER REVIEWED**

Fire: Caution: All these products have a very low flash point: Use of water spray when fighting fire may be inefficient. Small fires: Dry chemical, CO2, water spray or regular foam. Large fires: Water spray, fog or regular foam. Do not use straight streams. Move containers from fire area if you can do it without risk. Fire involving tanks or car/trailer loads: Fight fire from maximum distance or use unmanned hose holders or monitor nozzles. Cool containers with flooding quantities of water until well after fire is out. Withdraw immediately in case of rising sound from venting safety devices or discoloration of tank. Always stay away from the ends of tanks. For massive fire, use unmanned hose holders or monitor nozzles; if this is impossible, withdraw from area and let fire burn.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-130]**PEER REVIEWED**

Spill or leak: Eliminate all ignition sources (no smoking, flares, sparks or flames in immediate area). All equipment used when handling the product must be grounded. Do not touch or walk through spilled material. Stop leak if you can do it without risk. Prevent entry into waterways, sewers, basements or confined areas. A vapor suppressing foam may be used to reduce vapors. Absorb or cover with dry earth, sand or other non-combustible material and transfer to containers. Use clean non-sparking tools to collect absorbed material. Large spills: Dike far ahead of liquid spill for later disposal. Water spray may reduce vapor; but may not prevent ignition in closed spaces.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-130]**PEER REVIEWED**

First aid: Move victim to fresh air. Call emergency medical care. Apply artificial respiration if victim is not breathing. Administer oxygen if breathing is difficult. Remove and isolate contaminated clothing and shoes. In case of contact with substance, immediately flush skin or eyes with running water for at least 20 minutes. Wash skin with soap and water. Keep victim warm and quiet. Effects of exposure (inhalation, ingestion or skin contact) to substance may be delayed. Ensure that medical personnel are aware of the

material(s) involved, and take precautions to protect themselves.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-130]**PEER REVIEWED**

Odor Threshold:

2.14 ppm (8 mg/cu m). Odor recognition level is reported as 1.03 to 140 ug/cu m.
[Cleland, J.G., G.L. Kingsbury. Multimedia Environmental Goals for Environmental Assessment. Volume 1. EPA-600/7-77-136a. Research Triangle Park, NC: EPA, Nov. 1977.,p. E-146]**PEER REVIEWED**

Odor in air= 1.30x10+11 mol/cu cm
[Fazzalari, F.A. (ed.). Compilation of Odor and Taste Threshold Values Data. ASTM Data Series DS 48A (Committee E-18). Philadelphia, PA: American Society for Testing and Materials, 1978. 158]**PEER REVIEWED**

Skin, Eye and Respiratory Irritations:

A human eye irritant. An experimental skin and severe eye irritant.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 3190]**PEER REVIEWED**

Fire Potential:

Flammable liquid. A very dangerous fire hazard when exposed to heat, flame, or oxidizers.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 3190]**PEER REVIEWED**

NFPA Hazard Classification:

Health: 2. 2= Materials that, on intense or continued (but not chronic) exposure, could cause temporary incapacitation or possible residual injury, including those requiring the use of respiratory protective equipment that has an independent air supply. These materials are hazardous to health, but areas may be entered freely if personnel are provided with full-face mask self-contained breathing apparatus that provides complete eye protection.
[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 325-87]**PEER REVIEWED**

Flammability: 3. 3= This degree includes Class IB and IC flammable liquids and materials that can be easily ignited under almost all normal temperature conditions. Water may be ineffective in controlling or extinguishing fires in such materials.

[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 325-87]**PEER REVIEWED**

Reactivity: 0. 0= This degree includes materials that are normally stable, even under fire exposure conditions, and that do not react with water. Normal fire fighting procedures may be used.
[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 325-87]**PEER REVIEWED**

Flammable Limits:

Lower flammable limit: 1.1% by volume; Upper flammable limit: 7.1% by volume
[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 325-87]**PEER REVIEWED**

Flash Point:

40 deg F (4 deg C) (Closed cup)
[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 325-87]**PEER REVIEWED**

16 deg C (Open cup)
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Autoignition Temperature:

896 DEG F (480 DEG C)
[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 325-87]**PEER REVIEWED**

Fire Fighting Procedures:

TO FIGHT FIRE, USE FOAM, CO2, DRY CHEMICAL.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 3190]**PEER REVIEWED**

Approach fire from upwind to avoid hazardous vapors and toxic decomposition
[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 49-127]**PEER REVIEWED**

If material on fire or involved in fire: Do not extinguish fire unless flow can be stopped or safely confined. Use water in flooding quantities as fog. Solid streams of water may spread fire. Cool all

affected containers with flooding quantities of water. Apply water from as far a distance as possible. Use foam, dry chemical, or carbon dioxide.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 1057]**PEER REVIEWED**

Toxic Combustion Products:

MODERATELY DANGEROUS; WHEN HEATED, EMITS TOXIC FUMES /WHICH/ CAN REACT VIGOROUSLY WITH OXIDIZING MATERIALS.
[Sax, N.I. Dangerous Properties of Industrial Materials. 6th ed. New York, NY: Van Nostrand Reinhold, 1984. 2588]**PEER REVIEWED**

Firefighting Hazards:

Vapor is heavier than air and may travel a considerable distance to a source of ignition and flash back.
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Flame speed equals 37 cm/sec.
[Environment Canada; Tech Info for Problem Spills: Toluene (Draft) p.3 (1979)]**PEER REVIEWED**

Explosive Limits & Potential:

LEL: 1.27%; UEL: 7%.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 3190]**PEER REVIEWED**

Hazardous Reactivities & Incompatibilities:

Frozen bromine trifluoride reacts violently with **toluene** at -80 deg C.
[Bretherick, L. Handbook of Reactive Chemical Hazards. 4th ed. Boston, MA: Butterworth-Heinemann Ltd., 1990 91]**PEER REVIEWED**

A mixture of /dinitrogen/ tetraoxide and **toluene** exploded, possibly initiated by impurities.
[Bretherick, L. Handbook of Reactive Chemical Hazards. 4th ed. Boston, MA: Butterworth-Heinemann Ltd., 1990 1353]**PEER REVIEWED**

Lack of proper control in nitration of **toluene** with mixed acids /nitric/ may lead to runaway or explosive reaction. A contributory factor is the oxidative formation, and subsequent nitration and decomposition of nitrocresols.
[Bretherick, L. Handbook of Reactive Chemical Hazards. 4th ed. Boston, MA: Butterworth-Heinemann Ltd., 1990 1165]**PEER REVIEWED**

When /tetranitromethane is/ mixed with hydrocarbons in approximately stoichiometric proportions, a sensitive highly explosive mixture is produced which needs careful handling ... . Explosion of only 10 g of a mixture with **toluene** caused 10 deaths and 20 severe injuries. The mixture contained excess **toluene**

in error.8
[Bretherick, L. Handbook of Reactive Chemical Hazards. 4th ed. Boston, MA: Butterworth-Heinemann Ltd., 1990 189]**PEER REVIEWED**

Interaction /of uranium hexafluoride/ with ... **toluene** ... is very vigorous, with separation of carbon, and violent with ethanol or water.
[Bretherick, L. Handbook of Reactive Chemical Hazards. 4th ed. Boston, MA: Butterworth-Heinemann Ltd., 1990 1126]**PEER REVIEWED**

Incompatible with strong oxidizers.
[Sittig, M. Handbook of Toxic and Hazardous Chemicals and Carcinogens, 1985. 2nd ed. Park Ridge, NJ: Noyes Data Corporation, 1985. 869]**PEER REVIEWED**

Strong oxidizers.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 310]**PEER REVIEWED**

Reacts photochemically with nitrogen oxides or halogens to form nitrotoluene, nitrobenzene and nitrophenol and halogenated products, respectively.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47 79 (1989)]**PEER REVIEWED**

Explosive reaction with 1,3-dichloro-5,5-dimethyl-2,4-imidazolididione; dinitrogen tetraoxide; concentrated nitric acid, sulfuric acid + nitric acid; N2O4; AgClO4; BrF3; Uranium hexafluoride; sulfur dichloride. Forms an explosive mixture with tetranitromethane.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 3190]**PEER REVIEWED**

Hazardous Decomposition:

When heated to decomposition it emits acrid smoke and irritating fumes.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 3190]**PEER REVIEWED**

Prior History of Accidents:

The wreck of the MV Ariadne, a Panamanian flag container ship, is examined as a case study of a hazardous substance emergency response in a third world country. /The ship/, carrying a cargo of heavy fuel oil, tetraethyl lead, xylene, **toluene**, methyl isobutyl ketone, butyl acetate, ethyl acetate, and acetone was grounded while departing the harbor of Mogadishu, Somalia. The Somalian government requested a team of technical advisors to help respond appropriately to the emergency. The major issues addressed by the advisory team were the need for additional salvage equipment and expertise, the danger of toxic fumes from the fire and explosions aboard the ship, the presence and possible release of tetraethyl lead,

possible port blockage by the wreck, recovery of the chemical drums, and the extent of environmental damage caused by the release of oil, pesticides, and tetraethyl lead into the harbor. ...
[Heare SF et al; 1986 Hazard Matl Spill Conf p.12-18 (1986)]**PEER REVIEWED**

Immediately Dangerous to Life or Health:

500 ppm
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 310]**PEER REVIEWED**

Protective Equipment & Clothing:

Protective clothing should include gloves, barrier creams, eye goggles or face shields, and a cartridge-type or self-contained breathing apparatus.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1332]**PEER REVIEWED**

WEAR SELF-CONTAINED BREATHING APPARATUS; WEAR GOGGLES IF EYE PROTECTION NOT PROVIDED.
[National Fire Protection Association. Fire Protection Guide on Hazardous Materials. 9th ed. Boston, MA: National Fire Protection Association, 1986.,p. 49-89]**PEER REVIEWED**

Eye protection: Glasses having shatter-resistant glass or equivalent lenses and side shields to protect the eyes from **toluene** splashes.
[NIOSH; Criteria Document: Toluene p.8 (1973) DHEW Pub. NIOSH 73-11023]**PEER REVIEWED**

If, for the purpose of maintenance or cleaning, a person is required to enter a vessel or similar area which has contained **toluene**, all suitable precautions for work in confined spaces should be adopted. Respiratory protection of the airline or self-contained type is essential; Reliance should not be placed on a canister respirator for such work. Workers whose hands may be exposed to **toluene** should wear suitable gloves or barrier creams. A thick layer of barrier cream should be applied. Under certain circumstances the use of a mask may be necessary for this type of work.
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 2185]**PEER REVIEWED**

Respirator selection: 500 ppm: Chemical cartridge respirator with organic vapor cartridge/supplied-air respirator/self-contained breathing apparatus; 1000 ppm: Chemical cartridge respirator with organic vapor cartridge with full facepiece; 2000 ppm: Gas mask with organic vapor canister/supplied-air respirator with full facepiece, helmet, or hood/self-contained breathing apparatus with full facepiece; Escape: gas mask with organic vapor canister/self-contained breathing apparatus.
[Sittig, M. Handbook of Toxic and Hazardous Chemicals and Carcinogens, 1985. 2nd ed. Park Ridge, NJ: Noyes Data Corporation, 1985. 870]**PEER REVIEWED**

Wear appropriate personal protective clothing to prevent skin contact.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 310]**PEER REVIEWED**

Wear appropriate eye protection to prevent eye contact.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 310]**PEER REVIEWED**

Recommendations for respirator selection. Max concn for use: 500 ppm. Respirator Class(es): Any chemical cartridge respirator with organic vapor cartridge(s). May require eye protection. Any powered, air-purifying respirator with organic vapor cartridge(s). May require eye protection. Any air-purifying, full-facepiece respirator (gas mask) with a chin-style, front- or back-mounted organic vapor canister. Any supplied-air respirator. May require eye protection. Any self-contained breathing apparatus with a full facepiece.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 310]**PEER REVIEWED**

Recommendations for respirator selection. Condition: Emergency or planned entry into unknown concn or IDLH conditions: Respirator Class(es): Any self-contained breathing apparatus that has a full facepiece and is operated in a pressure-demand or other positive-pressure mode. Any supplied-air respirator that has a full facepiece and is operated in a pressure-demand or other positive-pressure mode in combination with an auxiliary self-contained breathing apparatus operated in pressure-demand or other positive-pressure mode.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 310]**PEER REVIEWED**

Recommendations for respirator selection. Condition: Escape from suddenly occurring respiratory hazards: Respirator Class(es): Any air-purifying, full-facepiece respirator (gas mask) with a chin-style, front- or back-mounted organic vapor canister. Any appropriate escape-type, self-contained breathing apparatus.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 310]**PEER REVIEWED**

Preventive Measures:

Drench-type showers, eye-wash fountains should be installed and maintained to provide prompt, immediate access.
[NIOSH; Criteria Document: Toluene p.9 (1973) DHEW Pub. NIOSH 73-11023]**PEER REVIEWED**

Open lights or other agencies liable to ignite the vapor should be excluded from areas where the liquid is liable to be exposed in use or by accident.
[International Labour Office. Encyclopedia of Occupational Health and

Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 2185]**PEER REVIEWED**

A major concern in the painting studio is solvents, /including **toluene**/. ... Precautions include ... use of dilution and local exhaust ventilation, control of storage areas, disposal of solvent soaked rags in covered containers, minimizing skin exposure and the use of respirators and other personal protective equipment. The control of fire hazards is also important, since many of the solvents are highly flammable.
[Hart C; J Environ Health 49 (5): 282-86 (1987)]**PEER REVIEWED**

Contact lenses should not be worn when working with this chemical.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 310]**PEER REVIEWED**

SRP: The scientific literature for the use of contact lenses in industry is conflicting. The benefit or detrimental effects of wearing contact lenses depend not only upon the substance, but also on factors including the form of the substance, characteristics and duration of the exposure, the uses of other eye protection equipment, and the hygiene of the lenses. However, there may be individual substances whose irritating or corrosive properties are such that the wearing of contact lenses would be harmful to the eye. In those specific cases, contact lenses should not be worn. In any event, the usual eye protection equipment should be worn even when contact lenses are in place.
PEER REVIEWED

If material not on fire and not involved in fire: Keep sparks, flames, and other sources of ignition away. Keep material out of water sources and sewers. Build dikes to contain flow as necessary. Attempt to stop leak if without undue personnel hazard. Use water spray to knock-down vapors.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 1057]**PEER REVIEWED**

Personnel protection: Avoid breathing vapors. Keep upwind. ... Do not handle broken packages unless wearing appropriate personal protective equipment. Wash away any material which may have contacted the body with copious amounts of water or soap and water.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 1057]**PEER REVIEWED**

If material leaking (not on fire): Consider evacuation from downwind area based on amount of material spilled, location and weather conditions.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 1057]**PEER REVIEWED**

The worker should immediately wash the skin when it becomes contaminated.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 310]**PEER REVIEWED**

Work clothing that becomes wet should be immediately removed due to its flammability hazard.

[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 310]**PEER REVIEWED**

Shipment Methods and Regulations:

No person may /transport,/ offer or accept a hazardous material for transportation in commerce unless that person is registered in conformance ... and the hazardous material is properly classed, described, packaged, marked, labeled, and in condition for shipment as required or authorized by ... /the hazardous materials regulations (49 CFR 171-177)./
[49 CFR 171.2 (7/1/99)]**PEER REVIEWED**

The International Air Transport Association (IATA) Dangerous Goods Regulations are published by the IATA Dangerous Goods Board pursuant to IATA Resolutions 618 and 619 and constitute a manual of industry carrier regulations to be followed by all IATA Member airlines when transporting hazardous materials.
[IATA. Dangerous Goods Regulations. 40th Ed. Montreal, Canada and Geneva, Switzerland: International Air Transport Association, Dangerous Goods Regulations, 1999. 217]**PEER REVIEWED**

The International Maritime Dangerous Goods Code lays down basic principles for transporting hazardous chemicals. Detailed recommendations for individual substances and a number of recommendations for good practice are included in the classes dealing with such substances. A general index of technical names has also been compiled. This index should always be consulted when attempting to locate the appropriate procedures to be used when shipping any substance or article.
[IMDG; International Maritime Dangerous Goods Code; International Maritime Organization p.3285 (1998)]**PEER REVIEWED**

Storage Conditions:

Outside or detached storage is preferred. Inside storage should be in a standard flammable liquids storage warehouse, room, or cabinet. Separate from oxidizing materials.
[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 49-127]**PEER REVIEWED**

Use ambient storage temperature.
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Cleanup Methods:

Eliminate all ignition sources. Stop or control the leak, if this can be done without undue risk. Use water spray to cool and disperse vapors and protect personnel. Absorb in noncombustible material for proper disposal. Control runoff and isolate discharged material for proper disposal.
[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 49-197]**PEER REVIEWED**

1. REMOVE ALL IGNITION SOURCES. 2. VENTILATE AREA OF SPILL OR LEAK. 3. FOR SMALL QUANTITIES, ABSORB ON PAPER TOWELS. EVAPORATE IN SAFE PLACE (SUCH AS FUME HOOD). ALLOW SUFFICIENT TIME FOR EVAPORATING VAPORS TO COMPLETELY CLEAR HOOD DUCTWORK. BURN PAPER IN SUITABLE LOCATION AWAY FROM COMBUSTIBLE MATERIALS.
[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) PublicationNo. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981. 4]**PEER REVIEWED**

Fluorocarbon water foam may be used to diminish vapors and provide wet down.
[Environment Canada; Tech Info for Problem Spills: Toluene (Draft) p.94 (1982)]**PEER REVIEWED**

Cellosive and hycar absorbent materials, may be used for vapor suppression and/or containment of **toluene**.
[Environment Canada; Tech Info for Problem Spills: Toluene (Draft) p.94 (1982)]**PEER REVIEWED**

Treat contaminated water by gravity separation of solids, followed by skimming of surface. Pass through dual media filtration and carbon adsorption units (carbon ratio 1.0 kg to 10.0 kg soluble material). Return waste water from backwash to gravity separator.
[Environment Canada; Tech Info for Problem Spills: Toluene (Draft) p.94 (1982)]**PEER REVIEWED**

Environmental considerations - Land Spill: Dig a pit, pond, lagoon, holding area to contain liquid or solid material. /SRP: If time permits, pits, ponds, lagoons, soak holes, or holding areas should be sealed with an impermeable flexible membrane liner./ Dike surface flow using soil, sand bags, foamed polyurethane, or foamed concrete. Absorb bulk liquid with fly ash, cement powder,or commercial sorbents. Apply "universal" gelling agent to immobilize spill. Apply appropriate foam to diminish vapor and fire hazard.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 1057]**PEER REVIEWED**

Environmental considerations - Water Spill: Use natural barriers or oil spill control boom to limit spill travel. Use surface active agent (eg Detergent, soaps, alcohols), if approved by EPA. Inject "universal" gelling agent to solidify encircled spill and increase effectiveness of booms. If dissolved, in region of 10 ppm or greater concentration, apply activated carbon at ten times the spilled amount. Remove trapped material with suction hoses. Use mechanical dredges or lifts to remove immobilized masses of pollutants and precipitates.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 1057]**PEER REVIEWED**

Environmental considerations - Air Spill: Apply water spray or mist to knock down vapors.
[Association of American Railroads. Emergency Handling of Hazardous

Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 1057]**PEER REVIEWED**

Disposal Methods:

Generators of waste (equal to or greater than 100 kg/mo) containing this contaminant, EPA hazardous waste numbers U220, and F005 must conform with USEPA regulations in storage, transportation, treatment and disposal of waste.
[40 CFR 240-280, 300-306, 702-799 (7/1/90)]**PEER REVIEWED**

Toluene is a waste chemical stream constituent which may be subjected to ultimate disposal by controlled incineration.
[USEPA; Engineering Handbook for Hazardous Waste Incineration p.2-9 (1981) EPA 68-03-3025]**PEER REVIEWED**

A good candidate for liquid injection incineration at a temperature range of 650 to 1,600 deg C and a residence time of 0.1 to 2 seconds. A good candidate for rotary kiln incineration at a temperature range of 820 to 1,600 deg C and residence times of seconds for liquids and gases, and hours for solids. A good candidate for fluidized bed incineration at a temperature range of 450 to 980 deg C and residence times of seconds for liquids and gases, and longer for solids.
[USEPA; Engineering Handbook for Hazardous Waste Incineration p.3-16 (1981) EPA 68-03-3025]**PEER REVIEWED**

Additional flammable solvent may be added to increase incineration efficiency. Following treatment at a spill site or waste management facility, the resultant sludge can be disposed of to a secure landfill.
[Environment Canada; Tech Info for Problem Spills: Toluene (Draft) p.96 (1982)]**PEER REVIEWED**

LARGE QUANTITIES CAN BE RECLAIMED OR COLLECTED & ATOMIZED IN SUITABLE COMBUSTION CHAMBER. **TOLUENE** SHOULD NOT BE ALLOWED TO ENTER A CONFINED SPACE, SUCH AS SEWER, BECAUSE OF POSSIBILITY OF EXPLOSION. ... DISPOSAL METHODS: **TOLUENE** MAY BE DISPOSED OF BY ATOMIZING IN SUITABLE COMBUSTION CHAMBER.
[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) PublicationNo. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981. 4]**PEER REVIEWED**

The following wastewater treatment technologies have been investigated for **toluene**: biological treatment.
[USEPA; Management of Hazardous Waste Leachate, EPA Contract No.68-03-2766 p.E-48 (1982)]**PEER REVIEWED**

The following wastewater treatment technologies have been investigated for **toluene**: stripping.
[USEPA; Management of Hazardous Waste Leachate, EPA Contract No.68-03-2766 p.E-97 (1982)]**PEER REVIEWED**

The following wastewater treatment technologies have been investigated for **toluene**: solvent extraction.
[USEPA; Management of Hazardous Waste Leachate, EPA Contract

No.68-03-2766 p.E-112 (1982)]**PEER REVIEWED**

The following wastewater treatment technologies have been investigated for **toluene**: activated carbon.
[USEPA; Management of Hazardous Waste Leachate, EPA Contract No.68-03-2766 p.E-148 (1982)]**PEER REVIEWED**

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DOT Emergency Guidelines:

Fire or explosion: Highly flammable: Will be easily ignited by heat, sparks or flames. Vapors may form explosive mixtures with air. Vapors may travel to source of ignition and flash back. Most vapors are heavier than air. They will spread along ground and collect in low or confined areas (sewers, basements, tanks). Vapor explosion hazard indoors, outdoors or in sewers. Some may polymerize (P) explosively when heated or involved in a fire. Runoff to sewer may create fire or explosion hazard. Containers may explode when heated. Many liquids are lighter than water.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-130]**PEER REVIEWED**

Health: May cause toxic effects if inhaled or absorbed through skin. Inhalation or contact with material may irritate or burn skin and eyes. Fire will produce irritating, corrosive and/or toxic gases. Vapors may cause dizziness or suffocation. Runoff from fire control or dilution water may cause pollution.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-130]**PEER REVIEWED**

Public safety: Call Emergency Response Telephone Numbers. ... Isolate spill or leak area immediately for at least 50 to 100 meters (160 to 330 feet) in all directions. Keep unauthorized personnel away. Stay upwind. Keep out of low areas. Ventilate closed spaces before entering.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-130]**PEER REVIEWED**

Protective clothing: Wear positive pressure self-contained breathing apparatus (SCBA). Structural firefighters' protective clothing will only provide limited protection.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-130]**PEER REVIEWED**

Evacuation: Large spill: Consider initial downwind evacuation for at least 300 meters (1000 feet). Fire: If tank, rail car or tank truck is involved in a fire, isolate for 800 meters (1/2 mile) in all directions; also, consider initial evacuation for 800 meters (1/2 mile) in all directions.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-130]**PEER REVIEWED**

Fire: Caution: All these products have a very low flash point: Use of water spray when fighting fire may be inefficient. Small fires: Dry chemical, CO2, water spray or regular foam. Large fires: Water spray, fog or regular foam. Do not use straight streams. Move containers from fire area if you can do it without risk. Fire involving tanks or car/trailer loads: Fight fire from maximum distance or use unmanned hose holders or monitor nozzles. Cool containers with flooding quantities of water until well after fire is out. Withdraw immediately in case of rising sound from venting safety devices or discoloration of tank. Always stay away from the ends of tanks. For massive fire, use unmanned hose holders or monitor nozzles; if this is impossible, withdraw from area and let fire burn.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-130]**PEER REVIEWED**

Spill or leak: Eliminate all ignition sources (no smoking, flares, sparks or flames in immediate area). All equipment used when handling the product must be grounded. Do not touch or walk through spilled material. Stop leak if you can do it without risk. Prevent entry into waterways, sewers, basements or confined areas. A vapor suppressing foam may be used to reduce vapors. Absorb or cover with dry earth, sand or other non-combustible material and transfer to containers. Use clean non-sparking tools to collect absorbed material. Large spills: Dike far ahead of liquid spill for later disposal. Water spray may reduce vapor; but may not prevent ignition in closed spaces.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-130]**PEER REVIEWED**

First aid: Move victim to fresh air. Call emergency medical care. Apply artificial respiration if victim is not breathing. Administer oxygen if breathing is difficult. Remove and isolate contaminated clothing and shoes. In case of contact with substance, immediately flush skin or eyes with running water for at least 20 minutes. Wash skin with soap and water. Keep victim warm and quiet. Effects of exposure (inhalation, ingestion or skin contact) to substance may be delayed. Ensure that medical personnel are aware of the material(s) involved, and take precautions to protect themselves.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the

Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-130]**PEER REVIEWED**

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Odor Threshold:

2.14 ppm (8 mg/cu m). Odor recognition level is reported as 1.03 to 140 ug/cu m.
[Cleland, J.G., G.L. Kingsbury. Multimedia Environmental Goals for Environmental Assessment. Volume 1. EPA-600/7-77-136a. Research Triangle Park, NC: EPA, Nov. 1977.,p. E-146]**PEER REVIEWED**

Odor in air= 1.30x10+11 mol/cu cm
[Fazzalari, F.A. (ed.). Compilation of Odor and Taste Threshold Values Data. ASTM Data Series DS 48A (Committee E-18). Philadelphia, PA: American Society for Testing and Materials, 1978. 158]**PEER REVIEWED**

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Fire Potential:

Flammable liquid. A very dangerous fire hazard when exposed to heat, flame, or oxidizers.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 3190]**PEER REVIEWED**

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NFPA Hazard Classification:

Health: 2. 2= Materials that, on intense or continued (but not chronic) exposure, could cause temporary incapacitation or possible residual injury, including those requiring the use of respiratory protective equipment that has an independent air supply. These materials are hazardous to health, but areas may be entered freely if personnel are provided with full-face mask self-contained breathing apparatus that provides complete eye protection.
[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 325-87]**PEER REVIEWED**

Flammability: 3. 3= This degree includes Class IB and IC flammable liquids and materials that can be easily ignited under almost all normal temperature conditions. Water may be ineffective in controlling or extinguishing fires in such materials.
[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 325-87]**PEER REVIEWED**

Reactivity: 0. 0= This degree includes materials that are normally stable, even under fire exposure conditions, and that do not react with water. Normal fire fighting procedures may be used.
[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 325-87]**PEER REVIEWED**

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Flammable Limits:

Lower flammable limit: 1.1% by volume; Upper flammable limit: 7.1% by volume

[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 325-87]**PEER REVIEWED**

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Flash Point:

40 deg F (4 deg C) (Closed cup)

[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 325-87]**PEER REVIEWED**

16 deg C (Open cup)

[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

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Autoignition Temperature:

896 DEG F (480 DEG C)

[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 325-87]**PEER REVIEWED**

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Fire Fighting Procedures:

TO FIGHT FIRE, USE FOAM, CO2, DRY CHEMICAL.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 3190]**PEER REVIEWED**

Approach fire from upwind to avoid hazardous vapors and toxic decomposition
[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 49-127]**PEER REVIEWED**

If material on fire or involved in fire: Do not extinguish fire unless flow can be stopped or safely confined. Use water in flooding quantities as fog. Solid streams of water may spread fire. Cool all affected containers with flooding quantities of water. Apply water from as far a distance as possible. Use foam, dry chemical, or carbon dioxide.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 1057]**PEER REVIEWED**

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Toxic Combustion Products:

MODERATELY DANGEROUS; WHEN HEATED, EMITS TOXIC FUMES /WHICH/ CAN REACT VIGOROUSLY WITH OXIDIZING MATERIALS.
[Sax, N.I. Dangerous Properties of Industrial Materials. 6th ed. New York, NY: Van Nostrand Reinhold, 1984. 2588]**PEER REVIEWED**

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Firefighting Hazards:

Vapor is heavier than air and may travel a considerable distance to a source of ignition and flash back. [U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Flame speed equals 37 cm/sec. [Environment Canada; Tech Info for Problem Spills: Toluene (Draft) p.3 (1979)]**PEER REVIEWED**

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Explosive Limits & Potential:

LEL: 1.27%; UEL: 7%.

[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 3190]**PEER REVIEWED**

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Hazardous Reactivities & Incompatibilities:

Frozen bromine trifluoride reacts violently with **toluene** at -80 deg C.
[Bretherick, L. Handbook of Reactive Chemical Hazards. 4th ed. Boston, MA: Butterworth-Heinemann Ltd., 1990 91]**PEER REVIEWED**

A mixture of /dinitrogen/ tetraoxide and **toluene** exploded, possibly initiated by impurities.
[Bretherick, L. Handbook of Reactive Chemical Hazards. 4th ed. Boston, MA: Butterworth-Heinemann Ltd., 1990 1353]**PEER REVIEWED**

Lack of proper control in nitration of **toluene** with mixed acids /nitric/ may lead to runaway or explosive reaction. A contributory factor is the oxidative formation, and subsequent nitration and decomposition of nitrocresols.
[Bretherick, L. Handbook of Reactive Chemical Hazards. 4th ed. Boston, MA: Butterworth-Heinemann Ltd., 1990 1165]**PEER REVIEWED**

When /tetranitromethane is/ mixed with hydrocarbons in approximately stoichiometric proportions, a sensitive highly explosive mixture is produced which needs careful handling ... . Explosion of only 10 g of a mixture with **toluene** caused 10 deaths and 20 severe injuries. The mixture contained excess **toluene** in error.8
[Bretherick, L. Handbook of Reactive Chemical Hazards. 4th ed. Boston, MA: Butterworth-Heinemann Ltd., 1990 189]**PEER REVIEWED**

Interaction /of uranium hexafluoride/ with ... **toluene** ... is very vigorous, with separation of carbon, and violent with ethanol or water.
[Bretherick, L. Handbook of Reactive Chemical Hazards. 4th ed. Boston, MA: Butterworth-Heinemann Ltd., 1990 1126]**PEER REVIEWED**

Incompatible with strong oxidizers.
[Sittig, M. Handbook of Toxic and Hazardous Chemicals and Carcinogens, 1985. 2nd ed. Park Ridge, NJ: Noyes Data Corporation, 1985. 869]**PEER REVIEWED**

Strong oxidizers.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 310]**PEER REVIEWED**

Reacts photochemically with nitrogen oxides or halogens to form nitrotoluene, nitrobenzene and nitrophenol and halogenated products, respectively.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47 79 (1989)]**PEER REVIEWED**

Explosive reaction with 1,3-dichloro-5,5-dimethyl-2,4-imidazolididione; dinitrogen tetraoxide; concentrated nitric acid, sulfuric acid + nitric acid; N_2O_4; $AgClO_4$; BrF_3; Uranium hexafluoride; sulfur dichloride. Forms an explosive mixture with tetranitromethane.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 3190]**PEER REVIEWED**

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Hazardous Decomposition:

When heated to decomposition it emits acrid smoke and irritating fumes.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 3190]**PEER REVIEWED**

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Prior History of Accidents:

The wreck of the MV Ariadne, a Panamanian flag container ship, is examined as a case study of a hazardous substance emergency response in a third world country. /The ship/, carrying a cargo of heavy fuel oil, tetraethyl lead, xylene, **toluene**, methyl isobutyl ketone, butyl acetate, ethyl acetate, and acetone was grounded while departing the harbor of Mogadishu, Somalia. The Somalian government requested a team of technical advisors to help respond appropriately to the emergency. The major issues addressed by the advisory team were the need for additional salvage equipment and expertise, the danger of toxic fumes from the fire and explosions aboard the ship, the presence and possible release of tetraethyl lead, possible port blockage by the wreck, recovery of the chemical drums, and the extent of environmental damage caused by the release of oil, pesticides, and tetraethyl lead into the harbor. ...
[Heare SF et al; 1986 Hazard Matl Spill Conf p.12-18 (1986)]**PEER REVIEWED**

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Immediately Dangerous to Life or Health:

500 ppm

[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 310]**PEER REVIEWED**

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Protective Equipment & Clothing:

Protective clothing should include gloves, barrier creams, eye goggles or face shields, and a cartridge-type or self-contained breathing apparatus.
[Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994. 1332]**PEER REVIEWED**

WEAR SELF-CONTAINED BREATHING APPARATUS; WEAR GOGGLES IF EYE PROTECTION NOT PROVIDED.
[National Fire Protection Association. Fire Protection Guide on Hazardous Materials. 9th ed. Boston, MA: National Fire Protection Association, 1986.,p. 49-89]**PEER REVIEWED**

Eye protection: Glasses having shatter-resistant glass or equivalent lenses and side shields to protect the eyes from **toluene** splashes.
[NIOSH; Criteria Document: Toluene p.8 (1973) DHEW Pub. NIOSH 73-11023]**PEER REVIEWED**

If, for the purpose of maintenance or cleaning, a person is required to enter a vessel or similar area which has contained **toluene**, all suitable precautions for work in confined spaces should be adopted. Respiratory protection of the airline or self-contained type is essential; Reliance should not be placed on a canister respirator for such work. Workers whose hands may be exposed to **toluene** should wear suitable gloves or barrier creams. A thick layer of barrier cream should be applied. Under certain circumstances the use of a mask may be necessary for this type of work.
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 2185]**PEER REVIEWED**

Respirator selection: 500 ppm: Chemical cartridge respirator with organic vapor cartridge/supplied-air respirator/self-contained breathing apparatus; 1000 ppm: Chemical cartridge respirator with organic vapor cartridge with full facepiece; 2000 ppm: Gas mask with organic vapor canister/supplied-air respirator with full facepiece, helmet, or hood/self-contained breathing apparatus with full facepiece; Escape: gas mask with organic vapor canister/self-contained breathing apparatus.
[Sittig, M. Handbook of Toxic and Hazardous Chemicals and Carcinogens, 1985. 2nd ed. Park Ridge, NJ: Noyes Data Corporation, 1985. 870]**PEER REVIEWED**

Wear appropriate personal protective clothing to prevent skin contact.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 310]**PEER REVIEWED**

Wear appropriate eye protection to prevent eye contact.

[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 310]**PEER REVIEWED**

Recommendations for respirator selection. Max concn for use: 500 ppm. Respirator Class(es): Any chemical cartridge respirator with organic vapor cartridge(s). May require eye protection. Any powered, air-purifying respirator with organic vapor cartridge(s). May require eye protection. Any air-purifying, full-facepiece respirator (gas mask) with a chin-style, front- or back-mounted organic vapor canister. Any supplied-air respirator. May require eye protection. Any self-contained breathing apparatus with a full facepiece.

[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 310]**PEER REVIEWED**

Recommendations for respirator selection. Condition: Emergency or planned entry into unknown concn or IDLH conditions: Respirator Class(es): Any self-contained breathing apparatus that has a full facepiece and is operated in a pressure-demand or other positive-pressure mode. Any supplied-air respirator that has a full facepiece and is operated in a pressure-demand or other positive-pressure mode in combination with an auxiliary self-contained breathing apparatus operated in pressure-demand or other positive-pressure mode.

[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 310]**PEER REVIEWED**

Recommendations for respirator selection. Condition: Escape from suddenly occurring respiratory hazards: Respirator Class(es): Any air-purifying, full-facepiece respirator (gas mask) with a chin-style, front- or back-mounted organic vapor canister. Any appropriate escape-type, self-contained breathing apparatus.

[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 310]**PEER REVIEWED**

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Preventive Measures:

Drench-type showers, eye-wash fountains should be installed and maintained to provide prompt, immediate access.
[NIOSH; Criteria Document: Toluene p.9 (1973) DHEW Pub. NIOSH 73-11023]**PEER REVIEWED**

Open lights or other agencies liable to ignite the vapor should be excluded from areas where the liquid is liable to be exposed in use or by accident.
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 2185]**PEER REVIEWED**

A major concern in the painting studio is solvents, /including **toluene**/. ... Precautions include ... use of dilution and local exhaust ventilation, control of storage areas, disposal of solvent soaked rags in covered containers, minimizing skin exposure and the use of respirators and other personal protective equipment. The control of fire hazards is also important, since many of the solvents are highly flammable.
[Hart C; J Environ Health 49 (5): 282-86 (1987)]**PEER REVIEWED**

Contact lenses should not be worn when working with this chemical.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 310]**PEER REVIEWED**

SRP: The scientific literature for the use of contact lenses in industry is conflicting. The benefit or detrimental effects of wearing contact lenses depend not only upon the substance, but also on factors including the form of the substance, characteristics and duration of the exposure, the uses of other eye protection equipment, and the hygiene of the lenses. However, there may be individual substances whose irritating or corrosive properties are such that the wearing of contact lenses would be harmful to the eye. In those specific cases, contact lenses should not be worn. In any event, the usual eye protection equipment should be worn even when contact lenses are in place.
PEER REVIEWED

If material not on fire and not involved in fire: Keep sparks, flames, and other sources of ignition away. Keep material out of water sources and sewers. Build dikes to contain flow as necessary. Attempt to stop leak if without undue personnel hazard. Use water spray to knock-down vapors.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 1057]**PEER REVIEWED**

Personnel protection: Avoid breathing vapors. Keep upwind. ... Do not handle broken packages unless wearing appropriate personal protective equipment. Wash away any material which may have contacted the body with copious amounts of water or soap and water.
[Association of American Railroads. Emergency Handling of Hazardous

Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 1057]**PEER REVIEWED**

If material leaking (not on fire): Consider evacuation from downwind area based on amount of material spilled, location and weather conditions.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 1057]**PEER REVIEWED**

The worker should immediately wash the skin when it becomes contaminated.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 310]**PEER REVIEWED**

Work clothing that becomes wet should be immediately removed due to its flammability hazard.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 310]**PEER REVIEWED**

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Shipment Methods and Regulations:

No person may /transport,/ offer or accept a hazardous material for transportation in commerce unless that person is registered in conformance ... and the hazardous material is properly classed, described, packaged, marked, labeled, and in condition for shipment as required or authorized by ... /the hazardous materials regulations (49 CFR 171-177)./
[49 CFR 171.2 (7/1/99)]**PEER REVIEWED**

The International Air Transport Association (IATA) Dangerous Goods Regulations are published by the IATA Dangerous Goods Board pursuant to IATA Resolutions 618 and 619 and constitute a manual of industry carrier regulations to be followed by all IATA Member airlines when transporting hazardous materials.
[IATA. Dangerous Goods Regulations. 40th Ed. Montreal, Canada and Geneva, Switzerland: International Air Transport Association, Dangerous Goods Regulations, 1999. 217]**PEER REVIEWED**

The International Maritime Dangerous Goods Code lays down basic principles for transporting hazardous chemicals. Detailed recommendations for individual substances and a number of recommendations for good practice are included in the classes dealing with such substances. A general index of technical names has also been compiled. This index should always be consulted when attempting to locate the appropriate procedures to be used when shipping any substance or article.
[IMDG; International Maritime Dangerous Goods Code; International Maritime Organization p.3285 (1998)]**PEER REVIEWED**

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Storage Conditions:

Outside or detached storage is preferred. Inside storage should be in a standard flammable liquids storage warehouse, room, or cabinet. Separate from oxidizing materials.
[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 49-127]**PEER REVIEWED**

Use ambient storage temperature.
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

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Cleanup Methods:

Eliminate all ignition sources. Stop or control the leak, if this can be done without undue risk. Use water spray to cool and disperse vapors and protect personnel. Absorb in noncombustible material for proper disposal. Control runoff and isolate discharged material for proper disposal.
[Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997.,p. 49-197]**PEER REVIEWED**

1. REMOVE ALL IGNITION SOURCES. 2. VENTILATE AREA OF SPILL OR LEAK. 3. FOR SMALL QUANTITIES, ABSORB ON PAPER TOWELS. EVAPORATE IN SAFE PLACE (SUCH AS FUME HOOD). ALLOW SUFFICIENT TIME FOR EVAPORATING VAPORS TO COMPLETELY CLEAR HOOD DUCTWORK. BURN PAPER IN SUITABLE LOCATION AWAY FROM COMBUSTIBLE MATERIALS.
[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) PublicationNo. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981. 4]**PEER REVIEWED**

Fluorocarbon water foam may be used to diminish vapors and provide wet down.
[Environment Canada; Tech Info for Problem Spills: Toluene (Draft) p.94 (1982)]**PEER REVIEWED**

Cellosive and hycar absorbent materials, may be used for vapor suppression and/or containment of **toluene**.
[Environment Canada; Tech Info for Problem Spills: Toluene (Draft) p.94 (1982)]**PEER REVIEWED**

Treat contaminated water by gravity separation of solids, followed by skimming of surface. Pass through dual media filtration and carbon adsorption units (carbon ratio 1.0 kg to 10.0 kg soluble material). Return waste water from backwash to gravity separator.
[Environment Canada; Tech Info for Problem Spills: Toluene (Draft) p.94 (1982)]**PEER REVIEWED**

Environmental considerations - Land Spill: Dig a pit, pond, lagoon, holding area to contain liquid or solid material. /SRP: If time permits, pits, ponds, lagoons, soak holes, or holding areas should be sealed with an impermeable flexible membrane liner./ Dike surface flow using soil, sand bags, foamed polyurethane, or foamed concrete. Absorb bulk liquid with fly ash, cement powder,or commercial sorbents. Apply "universal" gelling agent to immobilize spill. Apply appropriate foam to diminish vapor and fire hazard.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 1057]**PEER REVIEWED**

Environmental considerations - Water Spill: Use natural barriers or oil spill control boom to limit spill travel. Use surface active agent (eg Detergent, soaps, alcohols), if approved by EPA. Inject "universal" gelling agent to solidify encircled spill and increase effectiveness of booms. If dissolved, in region of 10 ppm or greater concentration, apply activated carbon at ten times the spilled amount. Remove trapped material with suction hoses. Use mechanical dredges or lifts to remove immobilized masses of pollutants and precipitates.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 1057]**PEER REVIEWED**

Environmental considerations - Air Spill: Apply water spray or mist to knock down vapors.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994. 1057]**PEER REVIEWED**

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Disposal Methods:

Generators of waste (equal to or greater than 100 kg/mo) containing this contaminant, EPA hazardous waste numbers U220, and F005 must conform with USEPA regulations in storage, transportation, treatment and disposal of waste.
[40 CFR 240-280, 300-306, 702-799 (7/1/90)]**PEER REVIEWED**

Toluene is a waste chemical stream constituent which may be subjected to ultimate disposal by controlled incineration.
[USEPA; Engineering Handbook for Hazardous Waste Incineration p.2-9 (1981) EPA 68-03-3025]**PEER REVIEWED**

A good candidate for liquid injection incineration at a temperature range of 650 to 1,600 deg C and a residence time of 0.1 to 2 seconds. A good candidate for rotary kiln incineration at a temperature range of 820 to 1,600 deg C and residence times of seconds for liquids and gases, and hours for solids. A good candidate for fluidized bed incineration at a temperature range of 450 to 980 deg C and residence times of seconds for liquids and gases, and longer for solids.
[USEPA; Engineering Handbook for Hazardous Waste Incineration p.3-16 (1981) EPA 68-03-3025]**PEER REVIEWED**

Additional flammable solvent may be added to increase incineration efficiency. Following treatment at a spill site or waste management facility, the resultant sludge can be disposed of to a secure landfill.
[Environment Canada; Tech Info for Problem Spills: Toluene (Draft) p.96 (1982)]**PEER REVIEWED**

LARGE QUANTITIES CAN BE RECLAIMED OR COLLECTED & ATOMIZED IN SUITABLE COMBUSTION CHAMBER. **TOLUENE** SHOULD NOT BE ALLOWED TO ENTER A CONFINED SPACE, SUCH AS SEWER, BECAUSE OF POSSIBILITY OF EXPLOSION. ... DISPOSAL METHODS: **TOLUENE** MAY BE DISPOSED OF BY ATOMIZING IN SUITABLE COMBUSTION CHAMBER.
[Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) PublicationNo. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981. 4]**PEER REVIEWED**

The following wastewater treatment technologies have been investigated for **toluene**: biological treatment.
[USEPA; Management of Hazardous Waste Leachate, EPA Contract No.68-03-2766 p.E-48 (1982)]**PEER REVIEWED**

The following wastewater treatment technologies have been investigated for **toluene**: stripping.
[USEPA; Management of Hazardous Waste Leachate, EPA Contract No.68-03-2766 p.E-97 (1982)]**PEER REVIEWED**

The following wastewater treatment technologies have been investigated for **toluene**: solvent extraction.

[USEPA; Management of Hazardous Waste Leachate, EPA Contract No.68-03-2766 p.E-112 (1982)]**PEER REVIEWED**

The following wastewater treatment technologies have been investigated for **toluene**: activated carbon.
[USEPA; Management of Hazardous Waste Leachate, EPA Contract No.68-03-2766 p.E-148 (1982)]**PEER REVIEWED**

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Occupational Exposure Standards:

OSHA Standards:

Permissible Exposure Limit: Table Z-2 8-hr Time Weighted Avg: 200 ppm.
[29 CFR 1910.1000 (7/1/99)]**PEER REVIEWED**

Permissible Exposure Limit: Table Z-2 Acceptable Ceiling Concentration: 300 ppm.
[29 CFR 1910.1000 (7/1/99)]**PEER REVIEWED**

Permissible Exposure Limit: Table Z-2 Acceptable maximum peak above the acceptable ceiling concentration for an 8-hour shift. Concentration: 500 ppm. Maximum Duration: 10 minutes.
[29 CFR 1910.1000 (7/1/99)]**PEER REVIEWED**

Vacated 1989 OSHA PEL TWA 100 ppm (375 mg/cu m); STEL 150 ppm (560 mg/cu m) is still enforced in some states.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 372]**PEER REVIEWED**

Threshold Limit Values:

8 Hr Time Weighted Avg (TWA) 50 ppm, skin
[American Conference of Governmental Industrial Hygienists. TLVs and BEIs. Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. Cincinnati, OH. 2000. 67]**QC REVIEWED**

Biological Exposure Index (BEI): Hippuric acid in urine at end of shift is 1.65 g/g creatinine. The determinant is usually present in a significant amt in biological specimens collected from subjects who have not been occupationally exposed. Such background levels are incl in the BEI value. The determinant is nonspecific, since it is observed after exposure to some other chemicals. These nonspecific tests are preferred because they are easy to use and usually offer a better correlation with exposure than specific tests. In such instances, a BEI for a specific, less quantitative biological determinant is recommended as a confirmatory test.
[American Conference of Governmental Industrial Hygienists. TLVs and BEIs. Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. Cincinnati, OH. 2000. 101]**QC REVIEWED**

Biological Exposure Index (BEI) adoption (1998): **Toluene** in venous blood prior to last shift of workweek is 0.5 mg/l.
[American Conference of Governmental Industrial Hygienists. TLVs and BEIs. Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. Cincinnati, OH. 2000. 101]**QC

REVIEWED**

Excursion Limit Recommendation: Excursions in worker exposure levels may exceed three times the TLV-TWA for no more than a total of 30 min during a work day, and under no circumstances should they exceed five times the TLV-TWA, provided that the TLV-TWA is not exceeded.
[American Conference of Governmental Industrial Hygienists. TLVs and BEIs. Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. Cincinnati, OH. 2000. 6]**QC REVIEWED**

Biological Exposure Index (BEI): Determinant: o-Cresol in urine; Sampling Time: end of shift; BEI:0.5 mg/L. The determinant is usually present in a significant amt in biological specimens collected from subjects who have not been occupationally exposed. Such background levels are incl in the BEI value.
[American Conference of Governmental Industrial Hygienists. TLVs and BEIs. Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. Cincinnati, OH. 2000. 101]**QC REVIEWED**

A4. A4= Not classifiable as a human carcinogen.
[American Conference of Governmental Industrial Hygienists. TLVs and BEIs. Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. Cincinnati, OH. 2000. 67]**QC REVIEWED**

NIOSH Recommendations:

Recommended Exposure Limit: 10 Hr Time-Weighted Avg: 100 ppm (375 mg/cu m).
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 310]**PEER REVIEWED**

Recommended Exposure Limit: 15 Min Short-Term Exposure Limit: 150 ppm (560 mg/cu m).
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 310]**PEER REVIEWED**

Immediately Dangerous to Life or Health:

500 ppm
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 310]**PEER REVIEWED**

Other Occupational Permissible Levels:

Australia: 100 ppm, STEL 150 ppm (substance under review) (1990); Federal Republic of Germany: 100 ppm, short-term level 500 ppm, 30 min, twice per shift, Pregnancy group B, a risk of damage to the developing embryo or fetus must be considered to be probable (1992); Sweden: 80 ppm, short-term value 100 ppm, 15 min, planning of new plants or alterations of old ones, 50 ppm (1990); United Kingdom: 50

ppm, 10-min STEL 150 ppm, skin (1991).
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Volumes I,II, III. Cincinnati, OH: ACGIH, 1991. 1577]**PEER REVIEWED**

Emergency Response Planning Guidelines (ERPG): ERPG(1) 50 ppm (no more than mild, transient effects) for up to 1 hr exposure; ERPG(2) 300 ppm (without serious, adverse effects) for up to 1 hr exposure; ERPG(3) 1000 ppm (not life threatening) up to 1 hr exposure.
[American Industrial Hygiene Association. The AIHA 1999 Emergency Response Planning Guidelines and Workplace Environmental Exposure Level Guides Handbook.American Industrial Hygiene Association. Fairfax, VA 1999. 27]**PEER REVIEWED**

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[29 CFR 1910.1000 (7/1/99)]**PEER REVIEWED**

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[29 CFR 1910.1000 (7/1/99)]**PEER REVIEWED**

Vacated 1989 OSHA PEL TWA 100 ppm (375 mg/cu m); STEL 150 ppm (560 mg/cu m) is still enforced in some states.
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8 Hr Time Weighted Avg (TWA) 50 ppm, skin
[American Conference of Governmental Industrial Hygienists. TLVs and BEIs. Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. Cincinnati, OH. 2000. 67]**QC REVIEWED**

Biological Exposure Index (BEI): Hippuric acid in urine at end of shift is 1.65 g/g creatinine. The determinant is usually present in a significant amt in biological specimens collected from subjects who have not been occupationally exposed. Such background levels are incl in the BEI value. The determinant is nonspecific, since it is observed after exposure to some other chemicals. These nonspecific tests are preferred because they are easy to use and usually offer a better correlation with exposure than specific tests. In such instances, a BEI for a specific, less quantitative biological determinant is recommended as a confirmatory test.
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Biological Exposure Index (BEI) adoption (1998): **Toluene** in venous blood prior to last shift of workweek is 0.5 mg/l.
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Excursion Limit Recommendation: Excursions in worker exposure levels may exceed three times the TLV-TWA for no more than a total of 30 min during a work day, and under no circumstances should they exceed five times the TLV-TWA, provided that the TLV-TWA is not exceeded.
[American Conference of Governmental Industrial Hygienists. TLVs and BEIs. Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. Cincinnati, OH. 2000. 6]**QC REVIEWED**

Biological Exposure Index (BEI): Determinant: o-Cresol in urine; Sampling Time: end of shift; BEI:0.5 mg/L. The determinant is usually present in a significant amt in biological specimens collected from subjects who have not been occupationally exposed. Such background levels are incl in the BEI value.
[American Conference of Governmental Industrial Hygienists. TLVs and BEIs. Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. Cincinnati, OH. 2000. 101]**QC REVIEWED**

A4. A4= Not classifiable as a human carcinogen.

[American Conference of Governmental Industrial Hygienists. TLVs and BEIs. Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. Cincinnati, OH. 2000. 67]**QC REVIEWED**

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NIOSH Recommendations:

Recommended Exposure Limit: 10 Hr Time-Weighted Avg: 100 ppm (375 mg/cu m).
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 310]**PEER REVIEWED**

Recommended Exposure Limit: 15 Min Short-Term Exposure Limit: 150 ppm (560 mg/cu m).
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 310]**PEER REVIEWED**

TOLUENE

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Other Occupational Permissible Levels:

Australia: 100 ppm, STEL 150 ppm (substance under review) (1990); Federal Republic of Germany: 100 ppm, short-term level 500 ppm, 30 min, twice per shift, Pregnancy group B, a risk of damage to the developing embryo or fetus must be considered to be probable (1992); Sweden: 80 ppm, short-term value 100 ppm, 15 min, planning of new plants or alterations of old ones, 50 ppm (1990); United Kingdom: 50 ppm, 10-min STEL 150 ppm, skin (1991).
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Volumes I,II, III. Cincinnati, OH: ACGIH, 1991. 1577]**PEER REVIEWED**

Emergency Response Planning Guidelines (ERPG): ERPG(1) 50 ppm (no more than mild, transient effects) for up to 1 hr exposure; ERPG(2) 300 ppm (without serious, adverse effects) for up to 1 hr exposure; ERPG(3) 1000 ppm (not life threatening) up to 1 hr exposure.
[American Industrial Hygiene Association. The AIHA 1999 Emergency Response Planning Guidelines and Workplace Environmental Exposure Level Guides Handbook.American Industrial Hygiene Association. Fairfax, VA 1999. 27]**PEER REVIEWED**

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Manufacturing/Use Information:

Major Uses:

In manufacture benzoic acid, benzaldehyde, explosives, dyes, and many other organic compounds; as a solvent for paints, lacquers, gums, resins, in the extraction of various principles from plants; as gasoline additive.
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 1626]**PEER REVIEWED**

DILUENT FOR PHOTOGRAVURE INKS
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 2184]**PEER REVIEWED**

IN FABRIC & PAPER COATING, MFR ARTIFICIAL LEATHER
[Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965. 67]**PEER REVIEWED**

Used in cements, solvents, spot removers, cosmetics, antifreezes, and inks.
[Gleason MN; Chem Tox of Comm Prod, 3rd Ed, 1969 as cited in USEPA; Health Assessment Document: Toluene (Draft) (1982) EPA-600/8-82-008]**PEER REVIEWED**

Asphalt and naphtha constituent. Detergent manufacture.
[USEPA. Identification of Organic Cmpds in Effluents from Industrial Sources, (1975) EPA 560/3-75-002]**PEER REVIEWED**

Mfg benzene derivatives, caprolactam, saccharin, medicines, dyes, perfumes, TNT; solvent recovery plants; component of gasoline; solvent for paints and coatings, gums, resins, rubber and vinyl organosol; diluent and thinner in nitrocellulose lacquers; adhesive solvent in plastic toys and model airplanes; detergent mfg; gasoline and naphtha constituent.
[Verschueren, K. Handbook of Environmental Data on Organic Chemicals. 3rd ed. New York, NY: Van Nostrand Reinhold Co., 1996. 1722]**PEER REVIEWED**

Fuel blending
[ITII. Toxic and Hazardous Industrial Chemicals Safety Manual. Tokyo, Japan: The International Technical Information Institute, 1988. 525]**PEER REVIEWED**

DENATURANT
[SRI]**PEER REVIEWED**

The largest chemical use for **toluene** is the production of benzene and urethane via hydrodealkylation.
[CHEMICAL PRODUCTS SYNOPSIS: Toluene, 1985]**PEER REVIEWED**

Used in production of drugs of abuse.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 3190]**PEER REVIEWED**

Manufacturers:

Amoco Corp., 200 East Randolph Drive, Chicago, IL 60601, (312)856-6111; Production site: Texas City, TX 77590
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

BP America, 200 Public Square, Cleveland OH 44114-2375. (216) 586-4141; Production sites: Alliance, LA 70037; Lima, OH 45804
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

CITGO Petrochemical Co., 6130 S. Yale Ave., Tulsa, OK 74136, (918)495-4000; Production sites: Corpus Christi, TX 78469; Lake Charles, LA 70601; Lemont, IL 60439-3659
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Coastal Refining and Marketing, 9 Greenway Plaza, Houston, TX 77046, (713)877-6559; Production site: Corpus Christi, TX 78403
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Coastal Eagle Point Co., 9 PO Box 1000, US Route 130& I295 Westville, NJ 08093, (609)853-3100; Production site: Westville, NJ 08093
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Chevron Chemical Corp., 6001 Bollinger Canyon Rd., San Ramon, CA 94583, (925)842-5500; Production site: Port Arthur, TX 77460
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Dow Chemical USA, 2020 Dow Center, Midland, MI 48674, (517) 636-1000; Production site: Plaquemine, LA 70765
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Equistar Chemicals LP., One Houston Center, 1221 McKinney St., Suite 1600, Houston, TX 77010, (713)652-7300; Production sites: Alvin, TX 77511; Channelview, TX 77530; Corpus Christi, TX 78410
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Exxon Chemical Co., 13501 Katy Freeway, Houston, TX 77079, (281)871-6000; Production site: Baton Rouge, LA 70821
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Fina Oil and Chemical Co., PO Box 2159, Dallas, TX 75221-2159, (214) 750-2400; Production site: Port Arthur, TX 77460
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Hess Oil Virgin Islands Corp., Kings Hill Rd., P.O. Box 127 Kingshill, VI 00851-0127, (340)778-4000; Production site: St. Croix, VI 00850
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Koch Refining Co., PO Box 2256, Wichita, KS 67201, (316)828-5500; Production site: Corpus Christi, TX 78403
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Lyondell-CITGO Refining Co., 1200 Lawndale, Houston, TX 77017, (713)321-4111; Production site: Houston, TX 77252
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Marathon Ashland Petroleum LLC., 539 South Main St., Findlay, OH 45840-3295, (419) 422-2121; Production sites: Catlettsburg, KY 41129; Texas City, TX 77592-1191
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Mobil Chemical Co., 3225 Gallows Rd., Fairfax, VA 22037-0001, (703)846-3000; Production sites: Chalmette, LA 70043; Beaumont, TX 77704-3868
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Phillips Petroleum Co., Phillips Building, Bartlesville, OK 74004, (918)661-6600; Production site: Sweeney, TX 77480
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Phillips Puerto Rico Core Inc., Road 3 Route 710, Barrio Las Mareas Guayama PR 00785, (787)864-1515; Production site: Guayama, PR 00785
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Shell Chemical Co., One Shell Plaza, PO Box 2463, Houston, TX 77252-2463, (713)241-6161; Production site: Deer Park, TX 77536
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Sun Company Inc., 1801 Market St., Philadelphia, PA 19103, (800) 825-3535; Production sites: Marcus Hook, PA 19061; Toledo, OH 43693; Tulsa, OK 74102
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Texaco Refining and Marketing Inc., 10 Universal City Plaza, Universal City, CA 91608-1097, (818)505-2000; Production site: El Dorada, KS 67042
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Ultramar Diamond Corp., 6000 N. Loop 1604, W. San Antonio, TX 78249-1112, (210)592-2000; Production site: Three Rivers, TX 78071
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Valero Energy Corp., San Antonio Valero Tower, W 1H 10, San Antonio, TX 78229-4718, (210)370-2000; Production site: Houston, TX 77012-2408
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Methods of Manufacturing:

UNRECOVERED COMPONENT OF GASOLINE
[SRI]**PEER REVIEWED**

Catalytic reforming of petroleum steams accounts for 87% of total **toluene** production. An additional 9% is separated from pyrolysis gasoline produced in steam crackers during manufacture of ethylene and propylene ... coal-tar separation from coke ovens produces 1% of total **toluene** ... up to 2% of the **toluene** produced is obtained as a by-product from styrene manufacture.
[DCE/NCI; Monograph On Human Exposure To Chemicals In The Workplace: Toluene p.2-1 (1985)]**PEER REVIEWED**

(1) By catalytic reforming of petroleum. (2) By fractional distillation of coal tar light oil.
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 1997. 1113]**PEER REVIEWED**

General Manufacturing Information:

28th Highest-volume chemical produced in the USA (1995).
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 1997. 1113]**PEER REVIEWED**

Formulations/Preparations:

Research, reagent, nitration - all 99.8+%; Industrial: Contains 94+%, with 5% xylene and small amounts of benzene and nonaromatic hydrocarbons; 90/120: Less pure than industrial.
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Grades: Research 99.99%; Pure 99.98%
[Flick, E.W. Industrial Solvents Handbook. 3rd ed. Park Ridge, NJ: Noyes Publications, 1985. 48]**PEER REVIEWED**

Grades: 1st degree nitration; 2nd degree commercial; 90% solvent
[DCE/NCI; Monograph On Human Exposure To Chemicals In The Workplace: Toluene p.1-1 (1985)]**PEER REVIEWED**

Grade: (Usually defined in terms of boiling ranges) Pure, commercial, straw-colored, nitration, scintilation, industrial.
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 1997. 1113]**PEER REVIEWED**

Impurities:

... Commercial grades /of **toluene**/ usually contain small amounts of benzene as an impurity.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 3190]**PEER REVIEWED**

Technical grades (90-120 deg C boiling range) are less pure and may contain up to 25% benzene as well as other hydrocarbons.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47 80 (1989)]**PEER REVIEWED**

Commercial grades /of **toluene**/ can ... contain polynuclear aromatic hydrocarbons (PAH), including pyrene, fluoranthrene, and benzo[ghi]perylene.
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Volumes I,II, III. Cincinnati, OH: ACGIH, 1991. 1568]**PEER REVIEWED**

Consumption Patterns:

CHEM INT FOR BENZENE, 55.3%; SOLVENT, 25.7%; CHEM INT FOR **TOLUENE** DIISOCYANATE, 7.3%; CHEM INT FOR BENZOIC ACID, 2.5%; CHEM INT FOR BENZYL CHLORIDE, 1.5%; OTHER, 7.7% (1981 NON-GASOLINE USE)
[SRI]**PEER REVIEWED**

Benzene, 46%; gasoline blending, 37%; solvent, 8%; **toluene** diisocyanate, 7%; miscellaneous chemicals, 2% (1985) /estimate/
[CHEMICAL PRODUCTS SYNOPSIS: Toluene, 1985]**PEER REVIEWED**

In the USA in 1981, the use of **toluene** as a solvent was second only to its use in benzene production via hydrodemethylation and accounted for about 26% of nonfuel consumption.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International

Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47 82 (1989)]**PEER REVIEWED**

Of the estimated 3.3 million tons of **toluene** produced in the USA in 1980, 44% was used to make benzene, 34% to make gasoline, 10% in solvents, 6% to make **toluene** diisocyanate, and 6% for miscellaneous use.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47 82 (1989)]**PEER REVIEWED**

U. S. Production:

(1981) 4.68X10+12 G (ALL USES, 93% CHEM GRADE)
[US INTERNATIONAL TRADE COMMISSION, WASH, DC 20436; SOC SERIES C/P-82-1]**PEER REVIEWED**

(1977) 1.50X10+12 G
[SRI]**PEER REVIEWED**

(1982) 1.54X10+12 G
[SRI]**PEER REVIEWED**

(1985) 2.30X10+12 g
[USITC. SYN ORG CHEM-U.S. PROD/SALES 1985 p.19]**PEER REVIEWED**

(1990) 6.21 billion lb
[Chem & Engineering News 70 (15): 17 (4/13/92)]**PEER REVIEWED**

(1991) 6.30 billion lb
[Chem & Engineering News 71 (15): 11 (4/12/93)]**PEER REVIEWED**

(1992) 5.81 billion lb
[Chem & Engineering News 72 (15): 13 (4/11/94)]**PEER REVIEWED**

(1993) 6.38 billion lb
[Chem & Engineering News 72 (15): 13 (4/11/94)]**PEER REVIEWED**

(1993) 2.276572X10+9 kg
[United States International Trade Commission. Synthetic Organic Chemicals - United States Production and Sales, 1993. USITC Publication 2810, Nov. 1994. Washington, D.C.,p. 3-13]**PEER REVIEWED**

U. S. Imports:

(1978) 1.92X10+11 G
[SRI]**PEER REVIEWED**

(1983) 2.73X10+11 G
[SRI]**PEER REVIEWED**

(1985) 1.57X10+8 gal
[BUREAU OF THE CENSUS. U.S. IMPORTS FOR CONSUMPTION AND GENERAL IMPORTS 1985 p.1-547]**PEER REVIEWED**

U. S. Exports:

(1978) 3.65X10+11 G
[SRI]**PEER REVIEWED**

(1983) 1.15X10+11 G
[SRI]**PEER REVIEWED**

(1985) 2.82X10+7 gal
[BUREAU OF THE CENSUS. U.S. EXPORTS, SCHEDULE E, 1985 p.2-70]**PEER REVIEWED**

TOLUENE

CASRN: 108-88-3

For other data, click on the Table of Contents

Major Uses:

In manufacture benzoic acid, benzaldehyde, explosives, dyes, and many other organic compounds; as a solvent for paints, lacquers, gums, resins, in the extraction of various principles from plants; as gasoline additive.
[Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 1626]**PEER REVIEWED**

DILUENT FOR PHOTOGRAVURE INKS
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 2184]**PEER REVIEWED**

IN FABRIC & PAPER COATING, MFR ARTIFICIAL LEATHER
[Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965. 67]**PEER REVIEWED**

Used in cements, solvents, spot removers, cosmetics, antifreezes, and inks.
[Gleason MN; Chem Tox of Comm Prod, 3rd Ed, 1969 as cited in USEPA; Health Assessment Document: Toluene (Draft) (1982) EPA-600/8-82-008]**PEER REVIEWED**

Asphalt and naphtha constituent. Detergent manufacture.
[USEPA. Identification of Organic Cmpds in Effluents from Industrial Sources, (1975) EPA 560/3-75-002]**PEER REVIEWED**

Mfg benzene derivatives, caprolactam, saccharin, medicines, dyes, perfumes, TNT; solvent recovery plants; component of gasoline; solvent for paints and coatings, gums, resins, rubber and vinyl organosol; diluent and thinner in nitrocellulose lacquers; adhesive solvent in plastic toys and model airplanes; detergent mfg; gasoline and naphtha constituent.
[Verschueren, K. Handbook of Environmental Data on Organic Chemicals. 3rd ed. New York, NY: Van Nostrand Reinhold Co., 1996. 1722]**PEER REVIEWED**

Fuel blending
[ITII. Toxic and Hazardous Industrial Chemicals Safety Manual. Tokyo, Japan: The International Technical Information Institute, 1988. 525]**PEER REVIEWED**

DENATURANT
[SRI]**PEER REVIEWED**

The largest chemical use for **toluene** is the production of benzene and urethane via hydrodealkylation.
[CHEMICAL PRODUCTS SYNOPSIS: Toluene, 1985]**PEER REVIEWED**

Used in production of drugs of abuse.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 3190]**PEER REVIEWED**

TOLUENE

CASRN: 108-88-3

For other data, click on the Table of Contents

Manufacturers:

Amoco Corp., 200 East Randolph Drive, Chicago, IL 60601, (312)856-6111; Production site: Texas City, TX 77590
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

BP America, 200 Public Square, Cleveland OH 44114-2375. (216) 586-4141; Production sites: Alliance, LA 70037; Lima, OH 45804
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

CITGO Petrochemical Co., 6130 S. Yale Ave., Tulsa, OK 74136, (918)495-4000; Production sites: Corpus Christi, TX 78469; Lake Charles, LA 70601; Lemont, IL 60439-3659
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Coastal Refining and Marketing, 9 Greenway Plaza, Houston, TX 77046, (713)877-6559; Production site: Corpus Christi, TX 78403
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Coastal Eagle Point Co., 9 PO Box 1000, US Route 130& I295 Westville, NJ 08093, (609)853-3100; Production site: Westville, NJ 08093
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Chevron Chemical Corp., 6001 Bollinger Canyon Rd., San Ramon, CA 94583, (925)842-5500; Production site: Port Arthur, TX 77460
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Dow Chemical USA, 2020 Dow Center, Midland, MI 48674, (517) 636-1000; Production site: Plaquemine, LA 70765
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Equistar Chemicals LP., One Houston Center, 1221 McKinney St., Suite 1600, Houston, TX 77010, (713)652-7300; Production sites: Alvin, TX 77511; Channelview, TX 77530; Corpus Christi, TX 78410
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Exxon Chemical Co., 13501 Katy Freeway, Houston, TX 77079, (281)871-6000; Production site: Baton Rouge, LA 70821
[SRI. 1998 Directory of Chemical Producers - United States of America.

SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Fina Oil and Chemical Co., PO Box 2159, Dallas, TX 75221-2159, (214) 750-2400; Production site: Port Arthur, TX 77460
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Hess Oil Virgin Islands Corp., Kings Hill Rd., P.O. Box 127 Kingshill, VI 00851-0127, (340)778-4000; Production site: St. Croix, VI 00850
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Koch Refining Co., PO Box 2256, Wichita, KS 67201, (316)828-5500; Production site: Corpus Christi, TX 78403
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Lyondell-CITGO Refining Co., 1200 Lawndale, Houston, TX 77017, (713)321-4111; Production site: Houston, TX 77252
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Marathon Ashland Petroleum LLC., 539 South Main St., Findlay, OH 45840-3295, (419) 422-2121; Production sites: Catlettsburg, KY 41129; Texas City, TX 77592-1191
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Mobil Chemical Co., 3225 Gallows Rd., Fairfax, VA 22037-0001, (703)846-3000; Production sites: Chalmette, LA 70043; Beaumont, TX 77704-3868
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Phillips Petroleum Co., Phillips Building, Bartlesville, OK 74004, (918)661-6600; Production site: Sweeney, TX 77480
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Phillips Puerto Rico Core Inc., Road 3 Route 710, Barrio Las Mareas Guayama PR 00785, (787)864-1515; Production site: Guayama, PR 00785
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Shell Chemical Co., One Shell Plaza, PO Box 2463, Houston, TX 77252-2463, (713)241-6161; Production site: Deer Park, TX 77536
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Sun Company Inc., 1801 Market St., Philadelphia, PA 19103, (800) 825-3535; Production sites: Marcus Hook, PA 19061; Toledo, OH 43693; Tulsa, OK 74102

[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Texaco Refining and Marketing Inc., 10 Universal City Plaza, Universal City, CA 91608-1097, (818)505-2000; Production site: El Dorada, KS 67042
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Ultramar Diamond Corp., 6000 N. Loop 1604, W. San Antonio, TX 78249-1112, (210)592-2000; Production site: Three Rivers, TX 78071
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

Valero Energy Corp., San Antonio Valero Tower, W 1H 10, San Antonio, TX 78229-4718, (210)370-2000; Production site: Houston, TX 77012-2408
[SRI. 1998 Directory of Chemical Producers - United States of America. SRI International, Menlo Park, CA. 1998. 955]**PEER REVIEWED**

TOLUENE

CASRN: 108-88-3

For other data, click on the Table of Contents

Methods of Manufacturing:

UNRECOVERED COMPONENT OF GASOLINE

[SRI]**PEER REVIEWED**

Catalytic reforming of petroleum steams accounts for 87% of total **toluene** production. An additional 9% is separated from pyrolysis gasoline produced in steam crackers during manufacture of ethylene and propylene ... coal-tar separation from coke ovens produces 1% of total **toluene** ... up to 2% of the **toluene** produced is obtained as a by-product from styrene manufacture.

[DCE/NCI; Monograph On Human Exposure To Chemicals In The Workplace: Toluene p.2-1 (1985)]**PEER REVIEWED**

(1) By catalytic reforming of petroleum. (2) By fractional distillation of coal tar light oil.

[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 1997. 1113]**PEER REVIEWED**

TOLUENE

CASRN: 108-88-3

For other data, click on the Table of Contents

General Manufacturing Information:

28th Highest-volume chemical produced in the USA (1995).
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 1997. 1113]**PEER REVIEWED**

TOLUENE

CASRN: 108-88-3

For other data, click on the Table of Contents

Formulations/Preparations:

Research, reagent, nitration - all 99.8+%; Industrial: Contains 94+%, with 5% xylene and small amounts of benzene and nonaromatic hydrocarbons; 90/120: Less pure than industrial.
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Grades: Research 99.99%; Pure 99.98%
[Flick, E.W. Industrial Solvents Handbook. 3rd ed. Park Ridge, NJ: Noyes Publications, 1985. 48]**PEER REVIEWED**

Grades: 1st degree nitration; 2nd degree commercial; 90% solvent
[DCE/NCI; Monograph On Human Exposure To Chemicals In The Workplace: Toluene p.1-1 (1985)]**PEER REVIEWED**

Grade: (Usually defined in terms of boiling ranges) Pure, commercial, straw-colored, nitration, scintilation, industrial.
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 1997. 1113]**PEER REVIEWED**

TOLUENE

CASRN: 108-88-3

For other data, click on the Table of Contents

Impurities:

... Commercial grades /of **toluene**/ usually contain small amounts of benzene as an impurity.
[Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996. 3190]**PEER REVIEWED**

Technical grades (90-120 deg C boiling range) are less pure and may contain up to 25% benzene as well as other hydrocarbons.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47 80 (1989)]**PEER REVIEWED**

Commercial grades /of **toluene**/ can ... contain polynuclear aromatic hydrocarbons (PAH), including pyrene, fluoranthrene, and benzo[ghi]perylene.
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Volumes I,II, III. Cincinnati, OH: ACGIH, 1991. 1568]**PEER REVIEWED**

TOLUENE

CASRN: 108-88-3

For other data, click on the Table of Contents

Consumption Patterns:

CHEM INT FOR BENZENE, 55.3%; SOLVENT, 25.7%; CHEM INT FOR **TOLUENE** DIISOCYANATE, 7.3%; CHEM INT FOR BENZOIC ACID, 2.5%; CHEM INT FOR BENZYL CHLORIDE, 1.5%; OTHER, 7.7% (1981 NON-GASOLINE USE)
[SRI]**PEER REVIEWED**

Benzene, 46%; gasoline blending, 37%; solvent, 8%; **toluene** diisocyanate, 7%; miscellaneous chemicals, 2% (1985) /estimate/
[CHEMICAL PRODUCTS SYNOPSIS: Toluene, 1985]**PEER REVIEWED**

In the USA in 1981, the use of **toluene** as a solvent was second only to its use in benzene production via hydrodemethylation and accounted for about 26% of nonfuel consumption.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47 82 (1989)]**PEER REVIEWED**

Of the estimated 3.3 million tons of **toluene** produced in the USA in 1980, 44% was used to make benzene, 34% to make gasoline, 10% in solvents, 6% to make **toluene** diisocyanate, and 6% for miscellaneous use.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V47 82 (1989)]**PEER REVIEWED**

TOLUENE

CASRN: 108-88-3

For other data, click on the Table of Contents

U. S. Production:

(1981) 4.68X10+12 G (ALL USES, 93% CHEM GRADE)
[US INTERNATIONAL TRADE COMMISSION, WASH, DC 20436; SOC SERIES C/P-82-1]**PEER REVIEWED**

(1977) 1.50X10+12 G
[SRI]**PEER REVIEWED**

(1982) 1.54X10+12 G
[SRI]**PEER REVIEWED**

(1985) 2.30X10+12 g
[USITC. SYN ORG CHEM-U.S. PROD/SALES 1985 p.19]**PEER REVIEWED**

(1990) 6.21 billion lb
[Chem & Engineering News 70 (15): 17 (4/13/92)]**PEER REVIEWED**

(1991) 6.30 billion lb
[Chem & Engineering News 71 (15): 11 (4/12/93)]**PEER REVIEWED**

(1992) 5.81 billion lb
[Chem & Engineering News 72 (15): 13 (4/11/94)]**PEER REVIEWED**

(1993) 6.38 billion lb
[Chem & Engineering News 72 (15): 13 (4/11/94)]**PEER REVIEWED**

(1993) 2.276572X10+9 kg
[United States International Trade Commission. Synthetic Organic Chemicals - United States Production and Sales, 1993. USITC Publication 2810, Nov. 1994. Washington, D.C.,p. 3-13]**PEER REVIEWED**

TOLUENE

CASRN: 108-88-3

For other data, click on the Table of Contents

U. S. Imports:

(1978) 1.92X10+11 G
[SRI]**PEER REVIEWED**

(1983) 2.73X10+11 G
[SRI]**PEER REVIEWED**

(1985) 1.57X10+8 gal
[BUREAU OF THE CENSUS. U.S. IMPORTS FOR CONSUMPTION AND GENERAL IMPORTS 1985 p.1-547]**PEER REVIEWED**

TOLUENE

CASRN: 108-88-3

For other data, click on the Table of Contents

U. S. Exports:

(1978) 3.65X10+11 G
[SRI]**PEER REVIEWED**

(1983) 1.15X10+11 G
[SRI]**PEER REVIEWED**

(1985) 2.82X10+7 gal
[BUREAU OF THE CENSUS. U.S. EXPORTS, SCHEDULE E, 1985 p.2-70]**PEER REVIEWED**

TOLUENE

CASRN: 108-88-3

For other data, click on the Table of Contents

Laboratory Methods:

Clinical Laboratory Methods:

NIOSH Method: 8002. Analyte: **Toluene**. Specimen: Venous blood, after 2 or more hours of exposure. Procedure: Gas chromatography, hydrogen-air flame ionization detector. The precision/RSD is 0.098 (1 ug/ml blood) and the recovery is 0.93 @ 2 ug/ml blood. The working range is 1 to 600 ug/ml. Applicability: **Toluene** is commonly found in trace amounts in humans working in the paint spray industry. Interferences: Ethanol in excess of the stated range increased blood **toluene** concentration. When substances other than the analytes are present in the blood, record their identities to determine possible interferences.
[U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. 8002-1]**PEER REVIEWED**

A procedure for the determination of **toluene** in blood by the purge and trap method is described ... has a linear range which extends up to at least 1500 ug/l ... detection limit ... is estimated to be less than 7.5 ug/l ...
[Cocheo V et al; Am Ind Hyg Assoc 43 (12): 938-41 (1982)]**PEER REVIEWED**

An automated high performance liquid chromatographic method for the direct determination of urinary concentrations of p-methylhippuric acids, and metabolites of **toluene** is described. A mixed solution of 5 mM potassium phosphate monobasic/acetonitrile (90/10) was used as a mobile phase . The method is simple and specific. Urine can be analyzed without solvent extraction.
[Ogata M, Taguchi T; Int Arch Occup Environ Health 59 (3): 263-72 (1987)]**PEER REVIEWED**

Analytic Laboratory Methods:

Quantitative determination of 4 to 40 ppm **toluene** in water with precision of 10% using IR spectroscopy.
[Amer Water Works Assoc; Standard Methods for the Examination of Water and Waste Water 14th Ed (1976)]**PEER REVIEWED**

Quantitative method for detection of **toluene** in water by gas chromatography. Levels over 1 ppm can be detected.
[Amer Water Works Assoc; Standard Methods for the Examination of Water and Waste Water 14th Ed (1976)]**PEER REVIEWED**

TOLUENE WAS IDENTIFIED IN WASTE-CONTAMINATED SOIL AND CHEMICAL STILL BOTTOM EXTRACTS BY GC/FOURIER TRANSFORM INFRARED SPECTROMETRY.
[GURKA DF, BETOWSKI LD; ANAL CHEM 54: 1819 (1982)]**PEER REVIEWED**

TWENTY AQ INDUST EFFLUENTS CONTAINING POLLUTANTS WERE ANALYZED USING ISOTOPE DILN & GC/MASS SPECTROMETRY. **TOLUENE** WAS ONE OF THE POLLUTANTS. [COLBY BN ET AL; INTERNATIONAL ENVIRONMENT & SAFETY FEB: 8 (1982)]**PEER REVIEWED**

NIOSH Method 1500. Analyte: **Toluene**. Matrix: Air. Procedure: Gas chromatography hydrogen-air flame ionization detector. For **toluene** this method has an estimated detection limit of 0.001 to 0.01 mg/sample with capillary column/sample. The overall precision/RSD is 0.011. Applicability: This method is intended for determining the OSHA-regulated hydrocarbons included within the boiling point range of n-pentane through n-octane. Interferences: At high humidity, breakthrough volumes may be reduced by as much as 50%.
[U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. 1500-1]**PEER REVIEWED**

NIOSH Method 4000. Analyte: **Toluene**. Procedure: Gas chromatography, hydrogen-air flame ionization detector. For **toluene** this method has an estimated detection limit of 0.01 mg/sample. The overall precision/RSD is 0.022. Applicability: The working range is 13 to 660 ppm (50 to 2500 mg/cu m) for a 4 hr sample. Interferences: None identified.
[U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. 4000-1]**PEER REVIEWED**

NIOSH Method 1501. Analyte: **Toluene**. Matrix: Air. Procedure: Gas chromatography, hydrogen-air flame ionization detector. For **toluene** this method has an estimated detection limit of 0.001 to 0.01 mg/sample with capillary column/sample. The overall precision/RSD is 0.011. Applicability: This method is for peak, ceiling and TWA determinations of aromatic hydrocarbons. Interferences: Use of the recommended column will prevent interferences by alkanes (less or equal to C10).
[U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. 1501-1]**PEER REVIEWED**

EPA Method 524.1. Purge-and-Trap Gas Chromatography/Mass Spectrometry. The method is applicable for the determination of volatile organic compounds in water, finished drinking water, raw source water, or drinking water in any treatment stage. For **toluene** the method has a detection limit of 0.08 ug/l and a standard deviation of 4.1%.
[USEPA; Methods for the Determination of Organic Compounds in Finished Drinking Water and Raw Source Water (1986)]**PEER REVIEWED**

EPA Method 524.2. Purge-and-Trap Gas Chromatography/Mass Spectrometry for the determination of volatile aromatic compounds in water including finished drinking water, raw source water, and drinking

water in any treatment stage. For **toluene** the method has a detection limit of 0.11 ug/l and a relative standard deviation of 8.0% with a wide bore capillary column, and a method detection limit of 0.08 ug/l and a relative standard deviation of 5.9% with a narrow bore capillary column.
[USEPA; Methods for the Determinatioon of Organic Compounds in Finished Drinking Water and Raw Source Water (1986)]**PEER REVIEWED**

EPA Method 602. Purge-and-Trap Gas Chromatography with photoionization detection for the determination of purgeable aromatics including **toluene** in municipal and industrial discharges. Under the prescribed conditions for **toluene** the detection limit is 0.2 ug/l. The method is applicable for use in the concentration range from the method detection limit to 100 times that limit. Precision and method accuracy were found to be directly related to the concentration of the analyte essentially independent of the sample matrix.
[40 CFR 136 97/1/91)]**PEER REVIEWED**

EPA Method 624. Purge-and-Trap Gas Chromatography/Mass Spectrometry for the analysis of purgeable organics including **toluene** in the municipal and industrial discharges. Under the prescribed conditions, for **toluene** the method has a detection limit of 6.0 ug/l. Precision and method accuracy were found to be directly related to the concentration of the analyte and essentially independent of the sample matrix.
[40 CFR 136 (7/1/91)]**PEER REVIEWED**

EPA Method 1624. Isotope Dilution Purge-and-Trap Gas Chromatography/Mass Spectrometry. This method is applicable for the determination of volatile organic compounds in municipal and industrial discharges. By adding a known amount of a labeled compound to every sample prior to purging, a correction of recovery of the pollutant can be made. If labeled compounds are not available, an internal standard method is used. Under the prescribed conditions, for both the labeled, and unlabeled ethylbenzene the method has a minimum detection level 10 ug/l.The established acceptance performance criteria at 20 ug/l is 6.2 ug/l for the standard deviation of the recovery, with the average recovery of 14.5 to 28.7 ug/l and the labeled cmpd recovery ranging from 4 to 193%.
[40 CFR 136 (7/1/91)]**PEER REVIEWED**

EPA Method 8020. Direct Injection or Purge-and-Trap Gas Chromatograpy with photoionization detection for the determination of aromatic volatile organics including **toluene** in solid waste. Under the prescribed conditions, for **toluene** the method has a detection limit of 0.2 ug/l. Precision and method accuracy were found to be directly related to the concentration of the analyte and essentially independent of the sample matrix.
[USEPA; Test Methods for Evaluating Solid Waste SW-846 (1986)]**PEER REVIEWED**

EPA Method 8240. Gas Chromatography/Mass Spectrometry for the determination of volatile Organics. This method can be used to quantify most volatile organic compounds including **toluene** that have boiling points below 200 deg C and are insoluble or slightly soluble in water. The detection limit is not given. Precision and method accuracy were found to be directly related to the concentration of the analyte and essentially independent of the sample matrix.
[USEPA; Test Methods for Evaluating Solid Waste SW-846 (1986)]**PEER REVIEWED**

EPA Method 502.2: Purge-and-Trap Capillary Column Gas Chromatography with Photoionization and

Electrolytic Conductivity Detectors in Series. The method is applicable for the determination of volatile organic compounds in finished drinking water, raw source water, or drinking water in any treatment stage. For **toluene** the method has a detection limit of 0.01 ug/l, a percent recovery of 99%, and a standard deviation of 1.9 using the photoionization detector.
[USEPA; Methods for the Determination of Organic Compounds in Finished Drinking Water and Raw Source Water (1986)]**PEER REVIEWED**

EPA Method 502.1. Purge and Trap Gas Chromatography with a halogen-specific detector for the determination of halogenated volatile compounds including **toluene** in finished drinking water, raw source water, or drinking water in any treatment stage. Under the prescribed conditions for **toluene**, the method detection limit is 0.02 ug/l.
[USEPA; Methods for the Determination of Organic Compounds in Finished Drinking Water and Raw Source Water (1986)]**PEER REVIEWED**

AOB Method OA-002-1. Volatile Organic Compounds by GC/MS Analysis of Tenax/CMS Cartridge and Summa Canister Samples. No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VA-001-1. Volatile Organic Compounds (VOCs) in Air Sampled by Sorbent Tubes and Analyzed by Purge and Trap GC. No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VA-003-1. Volatile Organic Compounds (VOCs) in Air by Portable GC/PID. No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VA-005-1. Volatile Organic Compounds (VOCs) in Ambient Air by Purge and Trap Gas Chromatography. No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VA-006-1. Volatile Organic Compounds (VOCs) in Ambient Air by Direct Portable GC/PID. No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VA-007-1. Volatile Organic Compounds (VOCs) in Ambient Air by GC/PID, GC/PID/FID, or GC/FID. No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER

REVIEWED**

AOB Method VA-008-1. Volatile Organic Compounds (VOCs) in Ambient Air by Portable GC/PID with Direct Sampling via Pump and Sample Loop. No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VG-001-1. Volatile Organics in Soil Gas - Adsorbent Tube Method. No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VG-006-1. Volatile Organic Compounds (VOCs) in Ambient Air by Purge and Trap GC. No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VG-007-1. Halogenated and Aromatic Volatile Organic Compounds (VOCs) in Air and Soil Gas Sampled by Sorbent Tubes and Analyzed by Purge and Trap GC/ELCD/PID. No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VG-008-1 . Volatile Organic Compounds (VOCs) in Soil Gas sampled by Tenax Tubes and Analyzed by Thermal Desorption GC/PID/ELCD. No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VG-010-1. Volatile Organic Compounds (VOCs) in Soil Gas by Direct Portable GC. No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AREAL Method IP-1A . Determination of Volatile Organic Compounds (VOCs) in Indoor Air Using Stainless Steel Canisters. No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AREAL Method IP-1B . Determination of Volatile Organic Compounds (VOCs) in Indoor Air using Solid Absorbent Tubes. No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AREAL Method TO-1 . Determination of Volatile Organic Compounds in Ambient Air using Tenax Adsorption and Gas Chromatography/Mass Spectrometry (GC/MS). No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AREAL Method TO-2 . Determination of Volatile Organic Compounds In Ambient Air by Carbon Molecular Sieve Adsorption and Gas Chromatography/Mass Spectrometry (GC/MS). No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AREAL Method TO-14. Determination of Volatile Organic Compounds (VOCs) in Ambient Air using SUMMA Passivated Canister Sampling and Gas Chromatographic Analysis. No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

Sampling Procedures:

... Personal dosimeter type badge monitor collects organic vapors ... /for analysis/ using gas chromatographic techniques ... sampled over the range of 0.5 ppm-1100 ppm /organic vapors/
[Lautenberger WJ et al; Am Ind Hyg Assoc J 41 (10): 737-47 (1980)]**PEER REVIEWED**

NIOSH Method 1500. Analyte: **Toluene**. Matrix: Air. Sampler: Solid sorbent tube (coconut shell charcoal, 100 mg/50 mg). Flow Rate: 0.20 l/min. Sample Size: 8 liters. Shipment: No special precautions. Sample Stability: At least 2 weeks.
[U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. 1500-1]**PEER REVIEWED**

NIOSH Method 4000. Analyte: **Toluene**. Sampler: Passive (activated carbon). Shipment: Transfer sorbent to septum-capped vial; otherwise routine. Sample Stability: At least 2 weeks @ 25 deg C if stored in septum-capped vial.
[U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. 4000-1]**PEER REVIEWED**

NIOSH Method 8002. Analyte: **Toluene**. Specimen: Venous blood, after 2 or more hrs of exposure. Shipment: Air express @ 4 deg C. Sample Stability: Stable @ 4 deg C for 3 weeks.
[U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes

1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. 8002-1]**PEER REVIEWED**

NIOSH Method 1501. Analyte: **Toluene**. Matrix: Air. Sampler: Solid sorbent tube (coconut shell charcoal, 100 mg/50 mg). Flow Rate: Less or equal to 0.20. Sample Size: 8-liters. Shipment: No special precautions. Sample Stability: Not determined.
[U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. 1501-1]**PEER REVIEWED**

TOLUENE

CASRN: 108-88-3

For other data, click on the Table of Contents

Clinical Laboratory Methods:

NIOSH Method: 8002. Analyte: **Toluene**. Specimen: Venous blood, after 2 or more hours of exposure. Procedure: Gas chromatography, hydrogen-air flame ionization detector. The precision/RSD is 0.098 (1 ug/ml blood) and the recovery is 0.93 @ 2 ug/ml blood. The working range is 1 to 600 ug/ml. Applicability: **Toluene** is commonly found in trace amounts in humans working in the paint spray industry. Interferences: Ethanol in excess of the stated range increased blood **toluene** concentration. When substances other than the analytes are present in the blood, record their identities to determine possible interferences.
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[Cocheo V et al; Am Ind Hyg Assoc 43 (12): 938-41 (1982)]**PEER REVIEWED**

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[Ogata M, Taguchi T; Int Arch Occup Environ Health 59 (3): 263-72 (1987)]**PEER REVIEWED**

TOLUENE

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[GURKA DF, BETOWSKI LD; ANAL CHEM 54: 1819 (1982)]**PEER REVIEWED**

TWENTY AQ INDUST EFFLUENTS CONTAINING POLLUTANTS WERE ANALYZED USING ISOTOPE DILN & GC/MASS SPECTROMETRY. **TOLUENE** WAS ONE OF THE POLLUTANTS.
[COLBY BN ET AL; INTERNATIONAL ENVIRONMENT & SAFETY FEB: 8 (1982)]**PEER REVIEWED**

NIOSH Method 1500. Analyte: **Toluene**. Matrix: Air. Procedure: Gas chromatography hydrogen-air flame ionization detector. For **toluene** this method has an estimated detection limit of 0.001 to 0.01 mg/sample with capillary column/sample. The overall precision/RSD is 0.011. Applicability: This method is intended for determining the OSHA-regulated hydrocarbons included within the boiling point range of n-pentane through n-octane. Interferences: At high humidity, breakthrough volumes may be reduced by as much as 50%.
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[U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. 4000-1]**PEER REVIEWED**

NIOSH Method 1501. Analyte: **Toluene**. Matrix: Air. Procedure: Gas chromatography, hydrogen-air flame ionization detector. For **toluene** this method has an estimated detection limit of 0.001 to 0.01

mg/sample with capillary column/sample. The overall precision/RSD is 0.011. Applicability: This method is for peak, ceiling and TWA determinations of aromatic hydrocarbons. Interferences: Use of the recommended column will prevent interferences by alkanes (less or equal to C10).
[U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. 1501-1]**PEER REVIEWED**

EPA Method 524.1. Purge-and-Trap Gas Chromatography/Mass Spectrometry. The method is applicable for the determination of volatile organic compounds in water, finished drinking water, raw source water, or drinking water in any treatment stage. For **toluene** the method has a detection limit of 0.08 ug/l and a standard deviation of 4.1%.
[USEPA; Methods for the Determination of Organic Compounds in Finished Drinking Water and Raw Source Water (1986)]**PEER REVIEWED**

EPA Method 524.2. Purge-and-Trap Gas Chromatography/Mass Spectrometry for the determination of volatile aromatic compounds in water including finished drinking water, raw source water, and drinking water in any treatment stage. For **toluene** the method has a detection limit of 0.11 ug/l and a relative standard deviation of 8.0% with a wide bore capillary column, and a method detection limit of 0.08 ug/l and a relative standard deviation of 5.9% with a narrow bore capillary column.
[USEPA; Methods for the Determinatioon of Organic Compounds in Finished Drinking Water and Raw Source Water (1986)]**PEER REVIEWED**

EPA Method 602. Purge-and-Trap Gas Chromatography with photoionization detection for the determination of purgeable aromatics including **toluene** in municipal and industrial discharges. Under the prescribed conditions for **toluene** the detection limit is 0.2 ug/l. The method is applicable for use in the concentration range from the method detection limit to 100 times that limit. Precision and method accuracy were found to be directly related to the concentration of the analyte essentially independent of the sample matrix.
[40 CFR 136 97/1/91)]**PEER REVIEWED**

EPA Method 624. Purge-and-Trap Gas Chromatography/Mass Spectrometry for the analysis of purgeable organics including **toluene** in the municipal and industrial discharges. Under the prescribed conditions, for **toluene** the method has a detection limit of 6.0 ug/l. Precision and method accuracy were found to be directly related to the concentration of the analyte and essentially independent of the sample matrix.
[40 CFR 136 (7/1/91)]**PEER REVIEWED**

EPA Method 1624. Isotope Dilution Purge-and-Trap Gas Chromatography/Mass Spectrometry. This method is applicable for the determination of volatile organic compounds in municipal and industrial discharges. By adding a known amount of a labeled compound to every sample prior to purging, a correction of recovery of the pollutant can be made. If labeled compounds are not available, an internal standard method is used. Under the prescribed conditions, for both the labeled, and unlabeled ethylbenzene the method has a minimum detection level 10 ug/l.The established acceptance performance criteria at 20 ug/l is 6.2 ug/l for the standard deviation of the recovery, with the average recovery of 14.5 to 28.7 ug/l and the labeled cmpd recovery ranging from 4 to 193%.

[40 CFR 136 (7/1/91)]**PEER REVIEWED**

EPA Method 8020. Direct Injection or Purge-and-Trap Gas Chromatograpy with photoionization detection for the determination of aromatic volatile organics including **toluene** in solid waste. Under the prescribed conditions, for **toluene** the method has a detection limit of 0.2 ug/l. Precision and method accuracy were found to be directly related to the concentration of the analyte and essentially independent of the sample matrix.
[USEPA; Test Methods for Evaluating Solid Waste SW-846 (1986)]**PEER REVIEWED**

EPA Method 8240. Gas Chromatography/Mass Spectrometry for the determination of volatile Organics. This method can be used to quantify most volatile organic compounds including **toluene** that have boiling points below 200 deg C and are insoluble or slightly soluble in water. The detection limit is not given. Precision and method accuracy were found to be directly related to the concentration of the analyte and essentially independent of the sample matrix.
[USEPA; Test Methods for Evaluating Solid Waste SW-846 (1986)]**PEER REVIEWED**

EPA Method 502.2: Purge-and-Trap Capillary Column Gas Chromatography with Photoionization and Electrolytic Conductivity Detectors in Series. The method is applicable for the determination of volatile organic compounds in finished drinking water, raw source water, or drinking water in any treatment stage. For **toluene** the method has a detection limit of 0.01 ug/l, a percent recovery of 99%, and a standard deviation of 1.9 using the photoionization detector.
[USEPA; Methods for the Determination of Organic Compounds in Finished Drinking Water and Raw Source Water (1986)]**PEER REVIEWED**

EPA Method 502.1. Purge and Trap Gas Chromatography with a halogen-specific detector for the determination of halogenated volatile compounds including **toluene** in finished drinking water, raw source water, or drinking water in any treatment stage. Under the prescribed conditions for **toluene**, the method detection limit is 0.02 ug/l.
[USEPA; Methods for the Determination of Organic Compounds in Finished Drinking Water and Raw Source Water (1986)]**PEER REVIEWED**

AOB Method OA-002-1. Volatile Organic Compounds by GC/MS Analysis of Tenax/CMS Cartridge and Summa Canister Samples. No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VA-001-1. Volatile Organic Compounds (VOCs) in Air Sampled by Sorbent Tubes and Analyzed by Purge and Trap GC. No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VA-003-1. Volatile Organic Compounds (VOCs) in Air by Portable GC/PID. No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version

1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VA-005-1. Volatile Organic Compounds (VOCs) in Ambient Air by Purge and Trap Gas Chromatography. No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VA-006-1. Volatile Organic Compounds (VOCs) in Ambient Air by Direct Portable GC/PID. No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VA-007-1. Volatile Organic Compounds (VOCs) in Ambient Air by GC/PID, GC/PID/FID, or GC/FID. No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VA-008-1. Volatile Organic Compounds (VOCs) in Ambient Air by Portable GC/PID with Direct Sampling via Pump and Sample Loop. No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VG-001-1. Volatile Organics in Soil Gas - Adsorbent Tube Method. No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VG-006-1. Volatile Organic Compounds (VOCs) in Ambient Air by Purge and Trap GC. No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VG-007-1. Halogenated and Aromatic Volatile Organic Compounds (VOCs) in Air and Soil Gas Sampled by Sorbent Tubes and Analyzed by Purge and Trap GC/ELCD/PID. No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AOB Method VG-008-1 . Volatile Organic Compounds (VOCs) in Soil Gas sampled by Tenax Tubes and Analyzed by Thermal Desorption GC/PID/ELCD. No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER

REVIEWED**

AOB Method VG-010-1. Volatile Organic Compounds (VOCs) in Soil Gas by Direct Portable GC. No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AREAL Method IP-1A . Determination of Volatile Organic Compounds (VOCs) in Indoor Air Using Stainless Steel Canisters. No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AREAL Method IP-1B . Determination of Volatile Organic Compounds (VOCs) in Indoor Air using Solid Absorbent Tubes. No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AREAL Method TO-1 . Determination of Volatile Organic Compounds in Ambient Air using Tenax Adsorption and Gas Chromatography/Mass Spectrometry (GC/MS). No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AREAL Method TO-2 . Determination of Volatile Organic Compounds In Ambient Air by Carbon Molecular Sieve Adsorption and Gas Chromatography/Mass Spectrometry (GC/MS). No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

AREAL Method TO-14. Determination of Volatile Organic Compounds (VOCs) in Ambient Air using SUMMA Passivated Canister Sampling and Gas Chromatographic Analysis. No detection limit.
[USEPA; EMMI. EPA's Environmental Monitoring Methods Index. Version 1.1. PC# 4082. Rockville, MD: Government Institutes (1997)]**PEER REVIEWED**

TOLUENE

CASRN: 108-88-3

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Sampling Procedures:

... Personal dosimeter type badge monitor collects organic vapors ... /for analysis/ using gas chromatographic techniques ... sampled over the range of 0.5 ppm-1100 ppm /organic vapors/ [Lautenberger WJ et al; Am Ind Hyg Assoc J 41 (10): 737-47 (1980)]**PEER REVIEWED**

NIOSH Method 1500. Analyte: **Toluene**. Matrix: Air. Sampler: Solid sorbent tube (coconut shell charcoal, 100 mg/50 mg). Flow Rate: 0.20 l/min. Sample Size: 8 liters. Shipment: No special precautions. Sample Stability: At least 2 weeks.
[U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. 1500-1]**PEER REVIEWED**

NIOSH Method 4000. Analyte: **Toluene**. Sampler: Passive (activated carbon). Shipment: Transfer sorbent to septum-capped vial; otherwise routine. Sample Stability: At least 2 weeks @ 25 deg C if stored in septum-capped vial.
[U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. 4000-1]**PEER REVIEWED**

NIOSH Method 8002. Analyte: **Toluene**. Specimen: Venous blood, after 2 or more hrs of exposure. Shipment: Air express @ 4 deg C. Sample Stability: Stable @ 4 deg C for 3 weeks.
[U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. 8002-1]**PEER REVIEWED**

NIOSH Method 1501. Analyte: **Toluene**. Matrix: Air. Sampler: Solid sorbent tube (coconut shell charcoal, 100 mg/50 mg). Flow Rate: Less or equal to 0.20. Sample Size: 8-liters. Shipment: No special precautions. Sample Stability: Not determined.
[U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. 1501-1]**PEER REVIEWED**

TOLUENE

CASRN: 108-88-3

For other data, click on the Table of Contents

Special References:

Special Reports:

REVIEW: BENIGNUS VA; NEUROTOXICOLOGY (PARK FOREST SOUTH, ILL) 2 (3): 567 (1981). REVIEW ON HEALTH EFFECTS OF **TOLUENE**, PARTICULARLY WITH RESPECT TO ITS NEUROTOXIC EFFECTS IN HUMANS AND LAB ANIMALS.

NIOSH; Criteria Document: **Toluene** (1973) DHEW Pub. NIOSH 73-11023

USEPA; Ambient Water Quality Doc: **Toluene** (1980) EPA 440/5-80-075

NAS/NRC; The Alkyl Benzenes 384 pp (1981)

USEPA; Health Assessment Document: **Toluene** (1982) EPA-800/8-82-008

TSCA CHIPs present a preliminary assessment of **toluene**'s potential for injury to human health & the environment (available at EPA's TSCA Assistance Office: (202) 554-1404.

Environment Canada; Tech Info for Problem Spills: **Toluene** (Draft) (1981)

Carlton WW et al; J Am Coll Toxicol 6 (1): 77-120 (1987). Final Report on the Safety Assessment of **Toluene**.

DHHS/ATSDR; Toxicological Profile for **Toluene** (Update) (1994) ATSDR/TP-93/14

DHHS/NTP; Toxicology & Carcinogenesis Studies of **Toluene** in F344/N Rats and B6C3F1 Mice Technical Report Series No. 371 (1990) NIH Publication No. 90-2826

TOLUENE

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TOLUENE

CASRN: 108-88-3

For other data, click on the Table of Contents

Synonyms and Identifiers:

Synonyms:

ANTISAL 1A
PEER REVIEWED

BENZENE, METHYL-
PEER REVIEWED

Caswell no 859
PEER REVIEWED

CP 25
PEER REVIEWED

METHACIDE
PEER REVIEWED

METHANE, PHENYL-
PEER REVIEWED

METHYLBENZENE
PEER REVIEWED

METHYLBENZOL
PEER REVIEWED

NCI-C07272
PEER REVIEWED

PHENYLMETHANE
PEER REVIEWED

TOLUEEN (DUTCH)
PEER REVIEWED

TOLUEN (CZECH)
PEER REVIEWED

TOLUOL
PEER REVIEWED

TOLUOLO (ITALIAN)
PEER REVIEWED

Formulations/Preparations:

Research, reagent, nitration - all 99.8+%; Industrial: Contains 94+%, with 5% xylene and small amounts of benzene and nonaromatic hydrocarbons; 90/120: Less pure than industrial.
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

Grades: Research 99.99%; Pure 99.98%
[Flick, E.W. Industrial Solvents Handbook. 3rd ed. Park Ridge, NJ: Noyes Publications, 1985. 48]**PEER REVIEWED**

Grades: 1st degree nitration; 2nd degree commercial; 90% solvent
[DCE/NCI; Monograph On Human Exposure To Chemicals In The Workplace: Toluene p.1-1 (1985)]**PEER REVIEWED**

Grade: (Usually defined in terms of boiling ranges) Pure, commercial, straw-colored, nitration, scintilation, industrial.
[Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 1997. 1113]**PEER REVIEWED**

Shipping Name/ Number DOT/UN/NA/IMO:

UN 1294; **Toluene**

IMO 3.2; **Toluene**

Standard Transportation Number:

49 093 05; **Toluene**

49 093 56; **Toluene** (**toluol**), reclaimed solvents, derived from the use of printing inks, consisting of 70% recycled **toluol** and not more than 30% lactol spirits, textile spirits and mineral spirits

49 060 10; **Toluene** (**toluol**), mixed with aluminum alkyls, not to exceed 20% (aluminum alkyl)

EPA Hazardous Waste Number:

U220; A toxic waste when a discarded commercial chemical product or manufacturing chemical intermediate or an off-specification commercial chemical product or manufacturing chemical intermediate.

F005; A hazardous waste from nonspecific sources when a spent solvent.

RTECS Number:

NIOSH/XS5250000

TOLUENE

CASRN: 108-88-3

For other data, click on the Table of Contents

Synonyms:

ANTISAL 1A
PEER REVIEWED

BENZENE, METHYL-
PEER REVIEWED

Caswell no 859
PEER REVIEWED

CP 25
PEER REVIEWED

METHACIDE
PEER REVIEWED

METHANE, PHENYL-
PEER REVIEWED

METHYLBENZENE
PEER REVIEWED

METHYLBENZOL
PEER REVIEWED

NCI-C07272
PEER REVIEWED

PHENYLMETHANE
PEER REVIEWED

TOLUEEN (DUTCH)
PEER REVIEWED

TOLUEN (CZECH)
PEER REVIEWED

TOLUOL
PEER REVIEWED

TOLUOLO (ITALIAN)
PEER REVIEWED

TOLUENE

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RTECS Number:

NIOSH/XS5250000

TOLUENE

CASRN: 108-88-3

For other data, click on the Table of Contents

Administrative Information:

Hazardous Substances Databank Number: 131

Last Revision Date: 20010131

Last Review Date: Reviewed by SRP on 1/29/2000

Update History:

Complete Update on 01/31/2001, 2 fields added/edited/deleted.
Complete Update on 09/12/2000, 1 field added/edited/deleted.
Complete Update on 08/04/2000, 91 fields added/edited/deleted.
Field Update on 06/12/2000, 1 field added/edited/deleted.
Field Update on 06/12/2000, 1 field added/edited/deleted.
Field Update on 02/02/2000, 1 field added/edited/deleted.
Field Update on 09/21/1999, 1 field added/edited/deleted.
Complete Update on 05/04/1999, 1 field added/edited/deleted.
Complete Update on 03/29/1999, 3 fields added/edited/deleted.
Field Update on 03/25/1999, 1 field added/edited/deleted.
Field Update on 03/19/1999, 1 field added/edited/deleted.
Complete Update on 02/24/1999, 1 field added/edited/deleted.
Complete Update on 01/20/1999, 3 fields added/edited/deleted.
Field Update on 12/18/1998, 1 field added/edited/deleted.
Complete Update on 11/12/1998, 1 field added/edited/deleted.
Complete Update on 09/11/1998, 1 field added/edited/deleted.
Complete Update on 06/02/1998, 1 field added/edited/deleted.
Complete Update on 03/25/1998, 4 fields added/edited/deleted.
Field Update on 02/25/1998, 1 field added/edited/deleted.
Field Update on 10/17/1997, 1 field added/edited/deleted.
Field Update on 09/08/1997, 5 fields added/edited/deleted.
Complete Update on 03/27/1997, 2 fields added/edited/deleted.
Complete Update on 02/26/1997, 1 field added/edited/deleted.
Complete Update on 06/11/1996, 1 field added/edited/deleted.
Complete Update on 05/10/1996, 1 field added/edited/deleted.
Complete Update on 04/18/1996, 2 fields added/edited/deleted.
Complete Update on 04/16/1996, 7 fields added/edited/deleted.
Complete Update on 01/18/1996, 1 field added/edited/deleted.
Complete Update on 06/09/1995, 1 field added/edited/deleted.
Complete Update on 05/26/1995, 1 field added/edited/deleted.
Complete Update on 01/24/1995, 1 field added/edited/deleted.
Complete Update on 12/19/1994, 1 field added/edited/deleted.
Complete Update on 11/18/1994, 2 fields added/edited/deleted.

Complete Update on 10/11/1994, 2 fields added/edited/deleted.
Complete Update on 09/13/1994, 2 fields added/edited/deleted.
Complete Update on 08/04/1994, 1 field added/edited/deleted.
Complete Update on 06/08/1994, 1 field added/edited/deleted.
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Complete Update on 03/25/1994, 1 field added/edited/deleted.
Complete Update on 09/15/1993, 1 field added/edited/deleted.
Complete Update on 08/17/1993, 1 field added/edited/deleted.
Complete Update on 08/07/1993, 1 field added/edited/deleted.
Complete Update on 08/04/1993, 1 field added/edited/deleted.
Complete Update on 04/30/1993, 1 field added/edited/deleted.
Complete Update on 02/05/1993, 1 field added/edited/deleted.
Field update on 12/11/1992, 1 field added/edited/deleted.
Complete Update on 11/20/1992, 1 field added/edited/deleted.
Complete Update on 09/18/1992, 1 field added/edited/deleted.
Complete Update on 09/14/1992, 73 fields added/edited/deleted.
Complete Update on 08/17/1992, 73 fields added/edited/deleted.
Field Update on 05/29/1992, 1 field added/edited/deleted.
Field Update on 04/16/1992, 1 field added/edited/deleted.
Field Update on 01/13/1992, 1 field added/edited/deleted.
Field Update on 09/10/1991, 1 field added/edited/deleted.
Complete Update on 07/08/1991, 1 field added/edited/deleted.
Complete Update on 05/31/1991, 1 field added/edited/deleted.
Complete Update on 10/22/1990, 9 fields added/edited/deleted.
Field Update on 05/14/1990, 1 field added/edited/deleted.
Field Update on 01/15/1990, 1 field added/edited/deleted.
Complete Update on 01/11/1990, 7 fields added/edited/deleted.
Field Update on 05/05/1989, 1 field added/edited/deleted.
Complete Update on 09/21/1988, 95 fields added/edited/deleted.
Complete Update on 05/31/1985

Record Length: 261364

TOLUENE

CASRN: 108-88-3

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Hazardous Substances Databank Number: 131

TOLUENE

CASRN: 108-88-3

For other data, click on the Table of Contents

Last Revision Date: 20010131

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CASRN: 108-88-3

For other data, click on the Table of Contents

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CASRN: 108-88-3

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Update History:

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Complete Update on 09/12/2000, 1 field added/edited/deleted.
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Complete Update on 03/29/1999, 3 fields added/edited/deleted.
Field Update on 03/25/1999, 1 field added/edited/deleted.
Field Update on 03/19/1999, 1 field added/edited/deleted.
Complete Update on 02/24/1999, 1 field added/edited/deleted.
Complete Update on 01/20/1999, 3 fields added/edited/deleted.
Field Update on 12/18/1998, 1 field added/edited/deleted.
Complete Update on 11/12/1998, 1 field added/edited/deleted.
Complete Update on 09/11/1998, 1 field added/edited/deleted.
Complete Update on 06/02/1998, 1 field added/edited/deleted.
Complete Update on 03/25/1998, 4 fields added/edited/deleted.
Field Update on 02/25/1998, 1 field added/edited/deleted.
Field Update on 10/17/1997, 1 field added/edited/deleted.
Field Update on 09/08/1997, 5 fields added/edited/deleted.
Complete Update on 03/27/1997, 2 fields added/edited/deleted.
Complete Update on 02/26/1997, 1 field added/edited/deleted.
Complete Update on 06/11/1996, 1 field added/edited/deleted.
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Complete Update on 04/18/1996, 2 fields added/edited/deleted.
Complete Update on 04/16/1996, 7 fields added/edited/deleted.
Complete Update on 01/18/1996, 1 field added/edited/deleted.
Complete Update on 06/09/1995, 1 field added/edited/deleted.
Complete Update on 05/26/1995, 1 field added/edited/deleted.
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Complete Update on 05/05/1994, 1 field added/edited/deleted.
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Complete Update on 04/30/1993, 1 field added/edited/deleted.
Complete Update on 02/05/1993, 1 field added/edited/deleted.
Field update on 12/11/1992, 1 field added/edited/deleted.
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Complete Update on 09/18/1992, 1 field added/edited/deleted.
Complete Update on 09/14/1992, 73 fields added/edited/deleted.
Complete Update on 08/17/1992, 73 fields added/edited/deleted.
Field Update on 05/29/1992, 1 field added/edited/deleted.
Field Update on 04/16/1992, 1 field added/edited/deleted.
Field Update on 01/13/1992, 1 field added/edited/deleted.
Field Update on 09/10/1991, 1 field added/edited/deleted.
Complete Update on 07/08/1991, 1 field added/edited/deleted.
Complete Update on 05/31/1991, 1 field added/edited/deleted.
Complete Update on 10/22/1990, 9 fields added/edited/deleted.
Field Update on 05/14/1990, 1 field added/edited/deleted.
Field Update on 01/15/1990, 1 field added/edited/deleted.
Complete Update on 01/11/1990, 7 fields added/edited/deleted.
Field Update on 05/05/1989, 1 field added/edited/deleted.
Complete Update on 09/21/1988, 95 fields added/edited/deleted.
Complete Update on 05/31/1985

TOLUENE

CASRN: 108-88-3

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Record Length: 261364

TOLUENE DIISOCYANATE

CASRN: 26471-62-5

For other data, click on the Table of Contents

Human Toxicity Excerpts:

The presence of different thresholds on bronchial reactivity to **toluene** diisocyanate was tested in 20 spray painters employed in the furniture industry and affected by TDI induced asthma. Bronchial provocation tests failed to demonstrate nonspecific hyperreactivity to methacholine. Exposure of the workers to **toluene** diisocyanate in concentrations ranging from 0.02 to 0.25 ppm demonstrated the occurrence of low, moderate and high thresholds of airways response to **toluene** diisocyanate in nine, seven and four patients, respectively. There was no association between the **toluene** diisocyanate response threshold and the positive response pattern to the lower range of **toluene** diisocyanate levels, but six of the nine patients with low threshold of response to **toluene** diisocyanate and six of the 11 patients with moderate or high thresholds had nonspecific bronchial hyperreactivity. The response to **toluene** diisocyanate also was not associated with the duration of the asthmatic condition, smoking, cessation of work or nonspecific response to methacholine. The pattern of response was not dose dependent in ten of 13 patients who had two positive bronchial provocation tests with different levels of **toluene** diisocyanate, although dual responses were recorded in three patients who had late reactions at low concentrations of **toluene** diisocyanate. The value of forced expiratory volume in one second, recorded during immediate reactions, showed a dose response relationship, in that it declined by 28.4% at lower **toluene** diisocyanate levels as compared to 38.3% following inhalation of higher doses of the compound; no such association was established for the late reaction to **toluene** diisocyanate. The results conclude that patients who are sensitive to **toluene** diisocyanate may have different thresholds of response to the agent.

[Paggiaro PL et al; Respiration 50 (3): 167-73 (1986)]**PEER REVIEWED**

TOLUENE DIISOCYANATE

CASRN: 26471-62-5

For other data, click on the Table of Contents

Non-Human Toxicity Excerpts:

Groups of 50 F344/N rats of each sex and 50 B6C3F1 mice of each sex were gavaged with corn oil or a mixture of **toluene** diisocyanate in corn oil for 5 days per wk for 105 or 106 wk. Female rats and mice were given doses of 60 or 120 mg/kg body weight, while male rats received 30 or 60 mg/kg, and male mice received 120 or 240 mg/kg. The **toluene** diisocyanate reacted with the moisture in the corn oil vehicle resulting in doses that were 10% to 23% below the target dose concn. The chemical product used was commercial grade **toluene** diisocyanate, which was an 80%-20% mixture of the 2,4- and 2,6-isomers. Chemical disposition and metabolism studies were conducted with each of the radiolabelled **toluene** diisocyanate isomers in male rats. Absorption of both of the **toluene** diisocyanate isomers occurred, with the highest concn found in the stomach, cecum, large intestine, and bladder. Excretion occurred via the feces and urine. The major metabolic products from the metabolism of 2,4-**toluene** diisocyanate were shown to be identical with those from the metabolism of the carcinogen, 2,4-diaminotoluene, whereas the metabolism of the 2,6-**toluene** diisocyanate isomer yielded one major product, identified as 2,6-bis(acetylamino)**toluene**. Greater than 10% depression in body weight gain occurred in all dosed groups of rats throughout most of the study. The major non-neoplastic lesions that were observed in both sexes of the **toluene** diisocyanate exposed rats were dose related incr in acute broncho-pneumonia, characterized as chemical pneumonitis, with incidences as high as 50%. In mice mean body weight gain was depressed in dosed male and in high dose females. The principle non-neoplastic lesion in mice that was attributed to chemical treatment was cytomegaly of the kidney tubular epithelium in males. Survival in all groups of dosed rats was significantly lower than in controls. A dose-dependent pattern of mortality did not commence until 70 wk of exposure, demonstrating that **toluene** diisocyanate elicited a cumulative toxic response. There was also significantly lower survival in high dose male, but not female mice, by comparison to controls. Despite the reduction of power and sensitivity in the rat studies caused by early mortality, statistically significant incr in tumor incidences were observed in many different target organs. **Toluene** diisocyanate was carcinogenic in F344/N rats, causing sc fibromas and fibrosarcomas in males and females, pancreatic acinar cell adenomas in males, and pancreatic islet cell adenomas, neoplastic nodules of the liver, and mammary gland tumors in females.

[Dieter MP et al; Toxicol Ind Health 6 (6): 599-621 (1990)]**PEER REVIEWED**

TOLUENE DIISOCYANATE

CASRN: 26471-62-5

For other data, click on the Table of Contents

Human Toxicity Excerpts:

Two men were exposed to **toluene** diisocyanate atmospheres at three different air concn (ca 25, 50 and 70 ug/cu m). The **toluene** diisocyanate atmospheres were generated by a gas-phase permeation method, and the exposures were performed in an 8-cu m stainless-steel test chamber. The effective exposure period was 4 hr. The isomeric composition of the air in the test chamber was 30% 2,4-**toluene** diisocyanate and 70% 2,6-**toluene** diisocyanate. The concn of **toluene** diisocyanate in air of the test chamber was determined by an HPLC method using the 9-(N-methyl-amino-methyl)-anthracene reagent and by a continuous-monitoring filter-tape instrument. Following the hydrolysis of plasma and urine, the related amines, 2,4-toluenediamine and 2,6-toluenediamine, were determined as pentafluoropropionic anhydride derivatives by capillary gas chromatography using selected ion monitoring in the electron impact mode. In plasma, 2,4- and 2,6-toluenediamine showed a rapid-phase elimination half-time of ca 2-5 hr, and that for the slow phase was greater than 6 days. A connection was observed between concn of 2,4- and 2,6-**toluene** diisocyanate in air and the levels of 2,4- and 2,6-toluenediamine in plasma. The cumulated amount of 2,4-toluenediamine excreted in the urine over 24 hr was ca 15%-19% of the estimated inhaled dose of 2,4-**toluene** diisocyanate, and that of 2,6-toluenediamine was ca 17%-23% of the inhaled dose of 2,6-**toluene** diisocyanate. A connection was found between the cumulated (24 hr) urinary excretion of 2,4- and 2,6-toluenediamine and the air concn of 2,4- and 2,6-**toluene** diisocyanate in the test chamber.

[Brorson T et al; Int Arch Occup Environ Health 63 (4): 253-9 (1991)]**PEER REVIEWED**

Best Sections

1 Synonyms
2 Synonyms
3 Synonyms
4 Synonyms
5 Non-Human Toxicity Excerpts
6 Human Toxicity Excerpts
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2,4-TOLUENE DIISOCYANATE

CASRN: 584-84-9

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Best Sections

Synonyms :

TOLUEEN-DIISOCYANAAT (DUTCH)
PEER REVIEWED

Synonyms :

TOLUEN-DISOCIANATO (ITALIAN)
PEER REVIEWED

Synonyms :

DIISOCYANAT-**TOLUOL** (GERMAN)
PEER REVIEWED

Synonyms :

2,4-DIISOCYANATO-1-**METHYLBENZENE**
PEER REVIEWED

Non-Human Toxicity Excerpts :

Groups of guinea pigs were exposed, via inhalation, to **toluene** diisocyanate concentrations ranging from 0.12 to 10 ppm. Exposure was for 3 hr/day on 5 consecutive days. Beginning on day 22, animals were evaluated for **toluene** diisocyanate specific antibodies, skin sensitivity, and pulmonary sensitivity to **toluene** diisocyanate. No antibodies were detected in animals exposed to 0.12 ppm **toluene** diisocyanate, whereas 55% of animals exposed to 0.36 ppm **toluene** diisocyanate or greater displayed **toluene** diisocyanate specific antibodies in their sera. Exposure to higher **toluene** diisocyanate concentrations resulted in both a greater percentage of animals producing antibodies and higher antibody titers. Pulmonary sensitivity, assessed by bronchial provocation challenge with **toluene** diisocyanate protein antigen, was not detected in animals exposed to 0.12 ppm **toluene** diisocyanate but was present in guinea pigs exposed to **toluene** diisocyanate concentrations of 0.36 ppm or greater. However, exposure concentrations higher than 2 ppm were pneumotoxic and resulted in few pulmonary hyprsensitivity reactions. Exposure of animals to 0.02 ppm **toluene** diisocyanate for 15 weeks did not result in either dermal sensitivity, pulmonary sensitivity, or production oftoluene diisocyanate specific antibody. The exposure protocol, as well as the exposure concentration, was important for establishment of sensitivity. Recognition of the concentration-response relationship governing immune reaction to inhaled **toluene** diisocyanate should permit establishment of safe airborne exposure levels for industrial workers to prevent sensitization. /**Toluene** diisocyanate/
[Karol MH; Toxicol Appl Pharmacol 68 (2): 229-41 (1983)]**PEER REVIEWED**

Human Toxicity Excerpts :

Ten sensitized subjects, previously shown to develop a dual or late asthmatic reaction after inhaling **toluene** diisocyanate were examined. In each subject, forced expiratory volume in one second was measured and venous blood was taken before, and 30 minutes and eight, 24, 48, and 72 hours after exposure to **toluene** diisocyanate (0.005-0.05 ppm for 10-30 minutes). Filtered air was used as a control. Differential leukocyte counts were determined and phenotypic analysis was performed by immunofluorescene on mononuclear cells using monoclonal antibodies

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(anti-CD3, anti-CD4, anti-CD8, and anti-HLA-DR). Five subjects developed a dual asthmatic reaction and five had a late reaction. Percentage of CD8 positive lymphocytes increased significantly eight hours after exposure to **toluene** diisocyanate (from 27 plus or minus 3 (SEM) % to 42.1 plus or minus 5%) in the subjects with an isolated late reaction. A delayed significant further increase in suppressor/cytotoxic T lymphocytes was seen in seven of the 10 subject 48 hours after active exposure (from 27 plus or minus 2% to 22 plus or minus 4.8%), irrespective of the type of asthmatic reaction developed after exposure to **toluene** diisocyanate. Eosinophil percentage increased from 2.5% plus or minus 1.0 to 6.4 plus or minus 1.2 24 hours after exposure to **toluene** diisocyante and the increase was sustained for up to 48 hours (4.7 plus or minus 1.1). No significant variations of forced expiratory volume in one second or cell percentages were seen in the controls. In conclusion, the events triggered by exposure to **toluene** diisocyante in sensitised subjects included changes in lung function and systemic effects which lasted longer than bronchoconstriction and concerned suppressor/cytotoxic lumphocytes and eosinophils. These results suggest that **toluene** diisocyanate induced late asthmatic reactions may be associated with an immunological response to **toluene** diisocyanate or to its products. /**Toluene** diisocyanate/
[Finotto S et al; Br J Ind Med 48 (2): 116-21 (1991)]**PEER REVIEWED**

Probable Routes of Human Exposure :

29,284 Workers are potentially exposed to 2,4-**toluene** diisocyanate based on statistical estimates derived from the NIOSH Survey conducted in 1972-1974 in the USA(1). This survey sampled 5000 businesses in 67 metropolitan areas throughout the US for the manufacture and use of chemicals, trade name products known to contain the compound and generic products suspected of containing the compound. 514 Workers are potentially exposed to 2,4-**toluene** diisocyanate based on statistical estimates derived from the NIOSH Survey conducted in 1981-1983 in the USA(2). Since the NOES survey excludes exposure to trade name chemicals which may contain the chemical, occupational exposure should be considerably higher(SRC). Airborne **toluene** diisocyanate in two plants producing flexible polyurethane foam for use in matresses, carpet pads, and air filters by a continuous slab process were determined(3). In this process the starting materials are mixed internally in a foaming nozzle and is poured onto moving kraft paper at which time the material foams and heats up (mixing end). The foam slab is then carried into a ventilated curing tunnel during which time the unreacted TDI and other material is driven off due to the high internal temperature (finishing end). The paper liner is subsequently stripped off and the slab cut into pieces. Concentration medians for 2,4-**toluene** diisocyanate were 0.70 and 0.33 ppb for the mixing and finishing ends, respectively(3). Only an insignificant number of samples exceeded the 20 ppb ceiling recommended by the ACGIH(3). In a similar Finish study, TDI vapor concentrations ranged from 25-80 ug/cu m for pouring, 14-44 ug/cu m for paper stripping, and 1-8 ug/cu m for cutting(4). Personal monitors measured 9-34 ug/cu m and 5-30 ug/cu m of the 2,4-isomer for pouring and paper stripping, respectively(4). While 2,4-**toluene** diisocyanate constitutes 80% of TDI, and 2,6-**toluene** diisocyanate 20%, the 2,4- isomer is more reactive so that the concentration of the 2,6-isomer is higher in workplace air(4). The percentage of 2,4-**toluene** diisocyanate to total **toluene** diisocyanate measured with the personal monitors ranged from 29 to 69%(4).
[(1) NIOSH; National Occupational Health Survey (1975) (2) NIOSH; National Occupational Exposure Survey (1985) (3) Rando RJ et al; Am Ind Hyg Assoc J 45: 199-203 (1984) (4) Rosenberg C, Savolainen H; J Chromatography 367: 385-92 (1986)]**PEER REVIEWED**

Non-Human Toxicity Excerpts :

Acetylcholinesterase activity was measured in bronchial tissue homogenate and blood from rats subjected to single and repeated 4 hr daily inhalation exposure to **toluene** diisocyanate or control atmospheres. A single 4 hr exposure to **toluene** diisocyanate in the concentration range of 0.7-4.3 ppm did not decrease AChE activity in bronchial tissue but a 4 hr exposure to 0.6 ppm **toluene** diisocyanate, or greater, for two consecutive days did reduce this activity (19% to 33% of the controls). Increasing the level of exposure to **toluene** diisocyanate for two consecutive days from 0.6 to 4.0 ppm and extending the length of exposure to 1.2 ppm **toluene** diisocyanate from 2 to 4, 9 or 14 days produced no further decrease in bronchial ACHE activity.

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Throughout these experiments, blood AChE activity remained unchanged. In rats exposed to 0.3 or 1 ppm **toluene** diisocyanate for 3 weeks, staining of the bronchial smooth muscle for AChE was reduced (36% of the controls) after exposure to 1 ppm **toluene** diisocyanate. These results support, for the first time, in vivo and localized anti-AChE activity by TDI. /**Toluene** diisocyanate/

[Brondeau MT et al; J Appl Toxicol 10 (6): 423-8 (1990)]**PEER REVIEWED**

Human Toxicity Excerpts :

A 41 yr old automobile paint sprayer showed the clinical features of hypersensitivity pneumonitis 1 wk after he had begun to work with paint material containing **toluene** diisocyanate. His symptoms (non-productive cough, dyspnea on exertion, and intermittent fever) began 6 to 8 hr after exposure to **toluene** diisocyanate and spontaneously disappeared by the next morning. He had diffuse, fine reticulonodular shadows on a chest roentgenogram and a restrictive impairment of pulmonary function. Immunoglobulin G antibody to **toluene** diisocyanate human serum albumin was present in bronchoalveolar lavage fluid and sera; IgA antibody was present only in bronchoalveolar lavage fluid. Also, the patient had sensitized bronchoalveolar lymphocytes to **toluene** diisocyanate human serum albumin. The histologic findings from a bronchial biopsy, showed an acute exudative reaction; the presence of alveolar edema and lymphocytic infiltrates in alveolar and bronchiolar walls, which suggested hypersensitivity pneumonitis. Bronchoalveolar lavage, which was repeated on four separate occasions showed lymphocytosis and a predominance of suppressor cytotoxic T cells. Findings from serial determination of humoral antibodies showed no changes consistent with the results of clinical and laboratory studies. In contrast, blastogenic responses of bronchoalveolar lymphocytes to **toluene** diisocyanate markedly decr, and the patient showed clinical improvement despite continued exposure to **toluene** diisocyanate. /**Toluene** diisocyanate/

[Yoshizawa Y et al; Ann Intern Med 110 (1): 31-4 (1989)]**PEER REVIEWED**

Human Toxicity Excerpts :

A case of building-related health complaints among 14 full-time employees and 1 part-time employee was investigated with respect to the relationship among frequency of symptoms (involving eyes, nose, sinuses, throat, lung, skeletomuscular system, and central nervous system) and antibodies to human serum albumin conjugates of **toluene** diisocyanate. Antibody testing was done by the ELISA procedure. Employees noted the presence or absence of symptoms by filling in questionnaires. Anti-**toluene** diisocyanate isotypes were found in 12 of 14 full-time employees and were nondetectable in one part-time employee. Antibody titers were positively but not significantly correlated with % of total symptoms as follows: **toluene** diisocyanate-IgG (r= 0.48), **toluene** diisocyanate-IgG (r= 0.55). Anti-**toluene** diisocyanate human serum albumin IgE titers were neg in 7 subjects and pos in 5. Anti-**toluene** diisocyanate human serum albumin-IgG antibodies were detected in all employees tested. /**Toluene** diisocyanate/

[Thrasher JD et al; Am J Ind Med 15 (2): 187-95 (1989)]**PEER REVIEWED**

Non-Human Toxicity Excerpts :

Toluene diisocyanate, a polymerizing agent used in production of plastics, can cause airway disease in some exposed individuals. Using guinea pigs as a model, the response of the airways and the type II cells of the peripheral lung was monitored morphologically and morphometrically after exposure to **toluene** diisocyanate vapors at 30 ppb, 260 ppb, and 3100 ppb. The two low doses of **toluene** diisocyanate caused little change in airways epithelium. There was not gross inflammatory cell infiltrate, however, surface infoldings and intracellular ciliated cysts increased in numbers. Animals exposed to 3100 ppb **toluene** diisocyanate 4 hr/day for 5 days, sustained considerable damage to the epithelium, and stratified nonkeratinizing cells lined the airways until ine week after exposure. Polymorphonuclear leukocytes were present in the early period after exposure. Increased numbers of eosinophils were present between one and two weeks following exposure. Mitoses in the epithelium were common during recovery. In the peripheral lung, though a modest subjective increase in the number of type II cells was seen after 3100 ppb **toluene** diisocyanate, the volume density of type II cells, and organellar

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Select Clear

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☐ Antidote and Emergency Treatment
☐ Animal Toxicity Studies

components (lamellar bodies, mitochondria, cisternal bodies) did not change significantly after any exposure level of **toluene** diisocyanate. /**Toluene** diisocyanate/
[Miller ML et al; Exp Lung Res 11 (2): 145-63 (1986)]**PEER REVIEWED**

Non-Human Toxicity Excerpts :

Guinea pigs were exposed by head only inhalation for 5 hr to concentrations of approximately 1 ppm of tolylene diisocyanate and 14 days later pinnal application of **toluene** diisocyanate on 3 consecutive days was followed by a dermal application of **toluene** diisocyanate after a further 7 days. The degree of contact sensitivity, measured 24 hr later, showed that prior inhalation inhibited the skin reaction to **toluene** diisocyanate but it did not change the skin reaction to chloro-dinitrobenzene in guinea pigs sensitized and challenged similarly with chloro-dinitrobenzene. The inhibition lasted up to 9 weeks. However, it did not occur in guinea pigs after intranasal instillation (instead of inhalation) and only occurred after oral dosage with **toluene** diisocyanate when the dose was relatively high. Treatment with cyclophosphamide before **toluene** diisocyanate inhalation reversed the inhibition of contact sensitivity, suggesting an involvement of suppressor cells. /**Toluene** diisocyanate/
[Doe J E et al; Int Arch Allergy Appl Immunol 68 (3): 275-9 (1982)]**PEER REVIEWED**

Human Toxicity Excerpts :

Radioallergosorbent testing was used to look for the presence of specific IgE antibody against a para-tolyl-monoisocyanate human serum albumin conjugate in sera from five groups of subjects. The first three groups consisted of individuals exposed to **toluene** diisocyanate who had been shown by bronchial provocation testing with levels of **toluene** diisocyanate below the threshold limit value of 0.02 ppm to have immediate asthmatic reactions, late asthmatic reactions or no resp changes at all. The two control groups consisted of atopic and non-atopic individuals who had no resp symptoms and no known exposure to **toluene** diisocyanate. Although radioallergosorbent showed high counts/min in some of the sera from patient with proven **toluene** diisocyanate induced resp disease, these levels were not significantly different from controls and appeared to reflect the presence in these sera of high levels of total IgE (greater than 100 u/ml). There is no evidence from this study for the presence of specific IgE antibody against a para-tolyl monoisocyanate human serum albumin conjugate in patients with **toluene** diisocyanate induced resp disease. /**Toluene** diisocyanate/
[Danks JM et al; Clin Allergy 11 (2): 161-8 (1981)]**PEER REVIEWED**

Human Toxicity Excerpts :

... Patients with **toluene** diisocyanate induced asthma continue to be symptomatic for month and even yr after cessation of **toluene** diisocyanate exposure. ... It is thought that **toluene** diisocyanate may cause the airways to become hyperreactive to many agents such as smoke and other air pollutants. ... Some individuals susceptible to **toluene** diisocyanate induced asthma develop cross-reactivity to other diisocyanate. ... /**Toluene** diisocyanate/
[Amdur, M.O., J. Doull, C.D. Klaasen (eds). Casarett and Doull's Toxicology. 4th ed. New York, NY: Pergamon Press, 1991. 305]**PEER REVIEWED**

Human Toxicity Excerpts :

The sera of 20 blood donors, 70 factory workers, and 1 casualty patient were assayed for IgE which bound to a p-tolyl-isocyanate human serum albumin conjugate. 3 factory workers had abnormally high assay values in assoc with active **toluene** diisocyanate disease, as indicated by asthma or measurement showing chronic airway obstruction. One factory worker had an exceptionally high assay value without clinical evidence of **toluene** diisocyanate disease. Hapten inhibition studies indicated possible heterogeneity of the IgE detected by the assay. Clinical histories suggest that **toluene** diisocyanate disease can incl susceptibility to asthma triggered by events other than **toluene** diisocyanate exposure. /**Toluene** diisocyanate/
[Game CJA; Am Ind Hyg Assoc J 43 (10): 759-63 (1982)]**PEER REVIEWED**

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- Non-Human Toxicity Excerpts
- Non-Human Toxicity Values
- TSCA Test Submissions
- Metabolism/Pharmacokinetics
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- Atmospheric Standards
- FDA Requirements
- Chemical/Physical Properties
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- Color/Form
- Odor
- Boiling Point
- Melting Point

Medical Surveillance :

A SCREENING PROGRAM WAS UNDERTAKEN AT A RESEARCH & DEVELOPMENT FACILITY OF A LARGE **TOLUENE** DIISOCYANATE MANUFACTURING CORPORATION. THE PURPOSE WAS TO DETERMINE THE OCCURRENCE OF ANTIBODIES TO **TOLUENE** DIISOCYANATE IN SELECTED WORKER POPULATIONS. NO TOLYL-REACTIVE IMMUNOGLOBULIN-E ANTIBODIES WERE DETECTED IN SERA WHEN WORKERS WERE EXPOSED ONLY TO AMBIENT **TOLUENE** DIISOCYANATE CONCN. WORKERS HAD ACUTE EXPOSURES TO **TOLUENE** DIISOCYANATE AS A RESULT OF SPILLS OR SPLASHES. ANTIBODY RESPONSES DEVELOPED IN 3 OF 4 INDIVIDUALS WHOSE ACUTE EXPOSURES WERE ACCOMPANIED BY IMMEDIATE RESPIRATORY SYMPTOMATOLOGY & A DECREASED FORCED EXPIRATORY VOLUME. AN ANTIBODY RESPONSE DEVELOPED IN 1 OF 9 WORKERS & IMMEDIATE RESPIRATORY SYMPTOMS, BUT NO SPIROMETRIC CHANGES UPON ACUTE TDI EXPOSURE. ROUTINE SEROLOGIC SCREENING OF WORKERS FOR TOLYL-REACTIVE ANTIBODIES MAY BE OF VALUE IN CONFIRMING SUSPECTED ISOCYANATE EXPOSURE & IN PROVIDING AN EARLY WARNING OF DEVELOPING TDI HYPERSENSITIVITY. /**TOLUENE** DIISOCYANATE/
[KAROL MH; J OCCUP MED 23 (11): 741 (1981)]**PEER REVIEWED**

Environmental Fate/Exposure Summary :

Commercial **toluene** diisocyanate (TDI) typically contains 80% of 2,4-**toluene** diisocyanate. It may be released to the environment as fugitive emissions and from stack exhaust during the production, transport, and use of TDI in the manufacture of polyurethane foam products and coatings as well as from spills. Much of the enviromental fate and monitoring data does not distinguish between the isomers of **toluene** diisocyanate, however, since the types of reactions are similar, some of the data presented below is for the commercial TDI mixture. The reactivity of the 2,4-**toluene** diisocyanate with compounds containing active hydrogen, such as water, alcohols or acids is greater than with the 2,6- isomer; therefore, the percentage of 2,4-**toluene** diisocyanate in monitored TDI is generally much less than 80% in the commercial mixture. If spilled on wet land, TDI is rapidly degraded. If released into water, a crust forms around the liquid TDI and < 0.5% of the original material remains after 35 days. Low concentrations of TDI hydrolyze in the aqueous environment in approximately a day. In the atmosphere, TDI reacts with photochemically produced hydroxyl radicals (half-life 3.3 hr) and is also removed by dry deposition. Human exposure is primarily occupational via inhalation and dermal contact. (SRC)
PEER REVIEWED

Mechanism of Action :

Guinea pigs were exposed to 29 ppb of **toluene** diisocyanate (97.8% 2,4- and 2.2% 2,6-) vapors 5 hr/day for 20 consecutive days. Animals were killed 20 hr after the last exposure, and tracheal smooth muscle relaxation and contraction responses to agonists were determined. There was no difference in beta-adrenergic responsiveness between the exposed animals and controls. Significant differences in carbachol-produced contractability were observed. The dose-effect curve from carbachol-stimulated strips was shifted upward and to the left for **toluene** diisocyanate exposed animals. The maximal smooth muscle tension was also greater in **toluene** diisocyanate exposed animals. The observed incr in maximal tension and the shift of the dose-effect curve for **toluene** diisocyanate exposed animals suggest a direct effect of **toluene** diisocyanate on tracheal smooth muscle.
[McKay RT, Brooks SM; Am Rev Respir Dis 129 (2): 296-300 (1984)]**PEER REVIEWED**

Cleanup Methods :

EFFECT OF WATER VAPOR ON ATMOSPHERIC **TOLUENE** DIISOCYANATE (TDI) WAS DETERMINED QUANTITATIVELY. AT 24 DEG C & ATMOSPHERIC PRESSURE MAX REDUCTION OF 50% WAS OBTAINED FOR INITIAL CONCN OF 0.4 & 0.034 PPM. THE DATA SUGGEST THAT INCR HUMIDITY WOULD BE ONLY MARGINALLY USEFUL AS A CONTROL METHOD. THEY DO, HOWEVER, EMPHASIZE THE NEED

- Density/Specific Gravity
- Heat of Combustion
- Solubilities
- Spectral Properties
- Surface Tension
- Vapor Density
- Vapor Pressure
- Other Chemical/Physical Properties
- Chemical Safety & Handling
- DOT Emergency Guidelines
- Odor Threshold
- Skin, Eye and Respiratory Irritations
- Fire Potential
- NFPA Hazard Classification
- Flammable Limits
- Flash Point
- Autoignition Temperature
- Fire Fighting Procedures
- Toxic Combustion Products
- Explosive Limits & Potential
- Hazardous Reactivities & Incompatibilities
- Hazardous Decomposition
- Hazardous Polymerization
- Immediately Dangerous to Life or Health
- Protective Equipment & Clothing
- Preventive Measures
- Stability/Shelf Life
- Shipment Methods and Regulations
- Storage Conditions
- Cleanup Methods
- Disposal Methods
- Occupational Exposure Standards
- OSHA Standards
- Threshold Limit Values
- NIOSH Recommendations
- Immediately Dangerous to Life or Health
- Other Occupational Permissible Levels

FOR SENSITIVE ANALYTICAL PROCEDURES TO MEASURE BOTH **TOLUENE** DIISOCYANATE AND THE **TOLUENE** DIISOCYANATE UREA AROUND THE TLV. /**TOLUENE** DIISOCYANATE/
[DYSON WL, HERMANN ER; AM IND HYG ASSOC J 32 (11): 741-4 (1971)]**PEER REVIEWED**

Non-Human Toxicity Excerpts :

Young adult guinea pigs received 2 open, epicutaneous induction applications (25 ul) of 8, 20 or 40% **toluene** diisocyanate in n-butyl ether on 2 separate areas. Five days later, animals were challenged with 0.0, 0.025, 0.05, 0.1, 0.2 and 0.4% TDI (25 ul/concn site). All challenge applications except the 0.0% soln elicited a positive response in 75-100% of the animals, and the severity of the skin reactions was dependent on the concn of the challenge and induction application. In another study using lower doses, animals received a total induction application (25 ul/each of 2 sites) of either 4 or 8% **toluene** diisocyanate. **Toluene** diisocyanate did not elicit a sensitization response at challenge concn up to 0.012% (total application of 3 ug) when a 4% induction application was used, while a challenge concn of 0.025% (total application of 6.25 ug) elicited a sensitization response in 63% of the animals. At the 8% induction application (total application of 4000 ug), all challenges, except the 0.0% indicated sensitization, and the intensities of the skin reactions were correlated with the challenge concn and the induction application. /**Toluene** diisocyanate/
[Koschier FJ et al; Toxicol Appl Pharmacol 67 (3): 401-7 (1983)]**PEER REVIEWED**

Human Toxicity Excerpts :

Toluene diisocyanate (TDI) sensitivity accompanied by nonspecific bronchial hyperresponsiveness occurs in approximately 5% of occupationally exposed workers. We report the case of a 32 yr old worker followed longitudinally after removal from isocyanate exposure. **Toluene** diisocyanate reactivity was lost 11 mo after removal from exposure and nonspecific bronchial hyperresponsiveness resolved after 17 mo. Bronchial reactivity to radishes (Raphanus sativus), which developed concurrently with **toluene** diisocyanate reactivity, was lost 2 yr later. Immunopharmacologic results show that the worker's initial decreased ability of lymphocytes to produce cyclic AMP returned to near normal after 2 yr. IgE antibodies to a human serum albumin tolyl monoisocyanate conjugate were still present at this time. /**Toluene** diisocyanate/
[Butcher BT et al; J Allergy Clin Immunol 70 (4): 231-5 (1982)]**PEER REVIEWED**

Emergency Medical Treatment :

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The following Overview, *** **TOLUENE**-2,4-DIISOCYANATE ***, is relevant for this HSDB record chemical.

Life Support:

- This overview assumes that basic life support measures have been instituted.

Clinical Effects:

- Manufacturing/Use Information
  - Major Uses
  - Manufacturers
  - Methods of Manufacturing
  - General Manufacturing Information
  - Formulations/Preparations
  - Impurities
  - Consumption Patterns
  - U. S. Production
  - U. S. Imports
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- Laboratory Methods
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- Synonyms and Identifiers
  - Synonyms
  - Formulations/Preparations
  - Shipping Name/ Number DOT/UN/NA/IMO
  - Standard Transportation Number
  - EPA Hazardous Waste Number
  - RTECS Number
- Administrative Information
  - Hazardous Substances Databank Number
  - Last Revision Date
  - Last Review Date
  - Update History
  - Record Length

SUMMARY OF EXPOSURE

0.2.1.1 ACUTE EXPOSURE

- **Toluene** diisocyanate (TDI) is an irritant to skin, lungs, conjunctiva and the mucous membranes of the gastrointestinal tract. Exposure can result in chemical pneumonitis, bronchospasm, bronchitis, and pulmonary edema; it is one of the leading causes of occupational asthma. Neurologic symptoms may include euphoria, loss of coordination, loss of consciousness, memory loss, and depression.

HEENT

0.2.4.1 ACUTE EXPOSURE

- Severe conjunctival irritation and lacrimation from liquid or high vapor concentrations is likely. Corneal edema may also occur. Lower concentrations may produce a burning or prickling sensation.

RESPIRATORY

0.2.6.1 ACUTE EXPOSURE

- Burning or irritation of the nose and throat, cough, laryngitis, chest pain, and asthmatic syndrome (chemical bronchitis with severe bronchospasm), sensation of oppression or constriction of the chest, bronchitis, pulmonary edema, and cor pulmonale may occur.
- Occupational asthma, emphysema, decreased pulmonary function, and hypersensitization may occur from chronic exposure.

NEUROLOGIC

0.2.7.1 ACUTE EXPOSURE

- Acute exposures may produce headache, insomnia, euphoria, ataxia, anxiety neurosis with depression, paranoid tendencies, or impotence.

GASTROINTESTINAL

0.2.8.1 ACUTE EXPOSURE

- Inhalation of vapor or aerosol may produce vomiting and abdominal pain. Epigastric and substernal pain may be secondary to the paroxysmal or persistent cough associated with inhalation.

HEMATOLOGIC

0.2.13.2 CHRONIC EXPOSURE

- Long-term effects may include blood cell damage and anemia.

DERMATOLOGIC

0.2.14.1 ACUTE EXPOSURE

- Irritation and inflammation are common. TDI is corrosive. Skin sensitization and allergic eczema may occur.

REPRODUCTIVE HAZARDS

- At the time of this review, no data were available to assess the teratogenic potential of this agent.
- At the time of this review, no data were available to assess the potential effects of exposure to this agent during pregnancy or lactation.

CARCINOGENICITY

0.2.21.1 IARC CATEGORY

- There is no data for evidence of carcinogenicity in humans; there is sufficient evidence in animals. It is rated as a 2B carcinogen by IARC (HSDB, 1998).

0.2.21.2 HUMAN OVERVIEW

- A 47 year old nonsmoking spray painter who had been exposed to **toluene** diisocyanate and 4,4-methylenediphenyl diisocyanate for 15 years developed an adenocarcinoma of the lung.
- A slight, but not significant, increase in rectal cancer and non- Hodgkin's lymphoma was found in workers in a polyurethane foam manufacturing plant.

0.2.21.3 ANIMAL OVERVIEW

- Rats and mice fed commercial grade **toluene** diisocyanate developed hemangiosarcomas in the liver, ovaries, and peritoneum; hepatocellular adenomas; pancreatic acinar cell adenomas; pancreatic islet cell adenomas; mammary gland tumors; and subcutaneous fibromas and fibrosarcomas.

GENOTOXICITY

- TDI induced mutations in S typhimurium and an increased incidence of sister chromatid exchanges occurred in Chinese hamster ovary cells. TDI did not induce chromosomal aberrations in Chinese hamster ovary cells.

Laboratory:

- Monitor respiratory function closely. Serum and urine toluenediamine levels should also be monitored.

Treatment Overview:

ORAL EXPOSURE

- Due to the irritant nature of this substance, emesis is not advised.
- GASTRIC LAVAGE: Consider after ingestion of a potentially life-threatening amount of poison if it can be performed soon after ingestion (generally within 1 hour). Protect airway by placement in Trendelenburg and left lateral decubitus position or by endotracheal intubation. Control any seizures first.
  1. CONTRAINDICATIONS: Loss of airway protective reflexes or decreased level of consciousness in unintubated patients; following ingestion of corrosives; hydrocarbons (high aspiration potential); patients at risk of hemorrhage or gastrointestinal perforation; and trivial or non-toxic ingestion.
- ACTIVATED CHARCOAL/CATHARTIC: Administer charcoal slurry, aqueous or mixed with saline cathartic or sorbitol. The FDA suggests 240 mL of diluent/30 g of charcoal. Usual charcoal dose is 25 to 100 grams in adults and adolescents, 25 to 50 grams in children (1 to 12 years old), and 1 gram/kilogram in infants less than 1 year old.
  1. Routine use of cathartics is NOT recommended. If used, administer only ONE dose of cathartic. Administer one dose of a cathartic, mixed with charcoal or given separately. See "Treatment: Prevention of Absorption" in the main document.
- Monitor patient for respiratory distress. If a cough or difficulty in breathing develops, evaluate for respiratory tract irritation, bronchitis and pneumonia.
- Allergic reaction - Sensitized individuals should be cautioned to avoid further exposure as serious allergic reactions may result.

- NOTE: See treatment of oral exposure in the main body of this document for complete information.

INHALATION EXPOSURE

- DECONTAMINATION: Move patient to fresh air. Monitor for respiratory distress. If cough or difficulty in breathing develops, evaluate for respiratory tract irritation, bronchitis, or pneumonitis. Administer 100 percent humidified supplemental oxygen with assisted ventilation as required.
- The specific role of bronchodilators for treatment of severe bronchoconstriction has not been evaluated. Asthma from TDI can be induced in the absence of airway hyperresponsiveness; in these cases bronchodilator use may contribute little to modifying severity.
- NOTE: See treatment of inhalation exposure in the main body of this document for complete information.

EYE EXPOSURE

- DECONTAMINATION: Exposed eyes should be irrigated with copious amounts of tepid water for at least 15 minutes. If irritation, pain, swelling, lacrimation, or photophobia persist, the patient should be seen in a health care facility.
- NOTE: See treatment of eye exposure in the main body of this document for complete information.

DERMAL EXPOSURE

- DECONTAMINATION: Wash exposed area extremely thoroughly with soap and water. A physician may need to examine the area if irritation or pain persists.
- NOTE: See treatment of dermal exposure in the main body of this document for complete information.

[Rumack BH: POISINDEX(R) Information System. Micromedex, Inc., Englewood, CO, 2001; CCIS Volume 107, edition exp February, 2001. Hall AH & Rumack BH (Eds):TOMES(R) Information System. Micromedex, Inc., Englewood, CO, 2001; CCIS Volume 107, edition exp February, 2001.] **PEER REVIEWED**

Human Toxicity Excerpts :

The outcome of the resp symptoms, pulmonary function tests and bronchial hyper-responsiveness was studied in 47 workers with resp disease due to **toluene** diisocyanate (27 asthmatic and 20 non-asthmatic subjects) after about 2 yr from the first exam. The data suggest that stopping occupational exposure to **toluene** diisocyanate frequently did not produce an improvement of the **toluene** diisocyanate bronchial asthma, and persistence of the exposure causes a more rapid decline in the resp function. /**Toluene** diisocyanate/
[Paggiaro PL et al; Clin Allergy 14 (5): 463-9 (1984)]**PEER REVIEWED**

Human Toxicity Excerpts :

The biconcave shape of normal human erythrocytes was altered into cup-shaped cells by **toluene** diisocyanate. The extent of **toluene** diisocyanate induced shape change of erythrocytes was concn-dependent. The resultant modified red cells had a decr ability to pass through a microporous membrane and also an incr resistance to hemolysis. Isolated membranes obtained from **toluene** diisocyanate treated cells showed incr crosslinking of membrane proteins and phospholipids. /**Toluene** diisocyanate/
[Manno S; Tokyo Joshi Ika Daigaku Zasshi 54 (7): 581-94 (1984)]**PEER REVIEWED**

Non-Human Toxicity Excerpts :

Allergic dermatitis was developed in mice by sensitization to **toluene** diisocyanate following which the mice were exposed to **toluene** diisocyanate vapor to see if a delayed type allergy plays a role in lung disorders caused by **toluene** diisocyanate. At a concn of 0.6 ppm, inhaled for 2 hr, allergic dermatitis did develop, but without noticeable pathological change in the resp organs. /**Toluene** diisocyanate/
[Ohsawa T; J Tokyo Women's Med Coll 53 (3): 237-46 (1983)]**PEER REVIEWED**

Medical Surveillance :

MEDICAL EVALUATIONS OF 15 WORKERS WERE MADE TO DETERMINE THE HEALTH EFFECTS OF EXPOSURE TO **TOLUENE** DIISOCYANATE PHOSGENE & **TOLUENE** DIISOCYANATE. THE FOLLOWING STEPS WERE RECOMMENDED: THE ENTIRE FACTORY POPULATION SHOULD BE SURVEYED PERIODICALLY FOR SYMPTOMS OF LOWER RESPIRATORY TRACT DISEASES & LUNG FUNCTION ABNORMALITIES THAT MAY BE CAUSED BY CHEMICAL EXPOSURE; **TOLUENE** DIISOCYANATE EXPOSURE SHOULD BE ENDED FOR SENSITIZED WORKERS OR FOR THOSE WITH EXCESSIVE DECLINE IN LUNG FUNCTION. /**TOLUENE** DIISOCYANATE/
[COSTELLO RJ, PETERS JM; HEALTH HAZARD EVALUATION DETERMINATION REPORT NO HE-78-31-623, OLIN CORPORATION, ASHTABULA, OHIO 44004; REPORT NIOSH-HE-78-31-623, ORDER NO PB80-195274 (1979)]**PEER REVIEWED**

Interactions :

2,4-**Toluene** diisocyanate exerted a nonspecific inhibitory effect on the beta-adrenergic adenylate cyclase system of frog erythrocyte membrane preparation stimulated by the beta-agonist isoproterenol in vitro. This inhibition was dose-dependent, ie, incr concn of **toluene** diisocyanate (TDI) produced progressively greater inhibition. The similarity in response between **toluene** diisocyanate and the isocyanates 1,6-diisocyanatohexane & diphenylmethane 4,4'-diisocyanate suggests that the isocyanate group plays a critical role in inhibiting the responsiveness of this system to beta-agonists.
[McKay T et al; Chest 80 (1, Suppl): 61-3 (1981)]**PEER REVIEWED**

Evidence for Carcinogenicity :

Evaluation: There is inadequate evidence for the carcinogenicity of **toluene** diisocyanates in humans. There is sufficient evidence for the carcinogenicity of **toluene** diisocyanates in experimental animals. Overall evaluation: **Toluene** diisocyanates are possibly carcinogenic to humans (Group 2B).
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. 71 876 (1999)]**PEER REVIEWED**

Absorption, Distribution & Excretion :

Inhalation of **toluene** diisocyanate results in toxic responses ranging from pulmonary irritation to immunological sensitization. The use of radioactively labeled isocyanate has made it possible to follow the initial uptake of the compound into the bloodstream independent of the final fate of the isocyanate. This study shows that the rate of uptake into the blood is linear during exposure to concentrations ranging from 0.00005 to 0.146 ppm and that the uptake continues to increase slightly postexposure. It also demonstrates that the radioactivity clears from the bloodstream to a level corresponding to approximately a 100 nM concentration of tolyl group after 72 hr and persists at a nanomolar level even 2 weeks following the exposure. This is similar to the response previously reported by this group for radioactively labeled methyl isocyanate. The initial ratre of (14)C uptake is also a linear function of the concentration of **toluene** diisocyanate when expressed either as concentration (ppm) or as concentration multiplied by duration of exposure (ppm/hr). This is discussed in comparison with the toxic responses as a function of both ppm and ppm/hr. Finally the inclusion of the data on methyl

isocyanate indicates that the uptake into arterial blood is a function of exposure concentration, independent of isocyanate structure. /**Toluene** diisocyanate/
[Kennedy AL et al; Toxicol Appl Pharmacol 100 (2): 280-92 (1989)]**PEER REVIEWED**

Mechanism of Action :

Non-specific bronchial reactivity to histamine has been measured before specific occupational bronchial tests in 51 workers exposed to **toluene** diisocyanate. The results showed that histamine reactivity was an important, but not obligatory, factor in the development of occupational asthma, and that it appeared to be the result rather than the cause of occupational asthma, as it returned towards normal in workers removed from exposure. **Toluene** diisocyanate was shown to be acting as a specific cause of occupational asthma rather than a non-specific irritant at a concn up to 0.02 ppm. /**Toluene** diisocyanate/
[Burge PS; Eur J Respir Dis (Suppl) 123: 91-6 (1982)]**PEER REVIEWED**

TSCA Test Submissions :

The mutagenicity of **toluene** 2,4-diisocyanate was evaluated in Salmonella tester strains TA98, TA100, TA1535, TA1537 and TA1538 (Ames Test), both in the presence and absence of metabolic activation by Aroclor-induced rat liver S9 fraction. Based on preliminary toxicity determinations, **toluene** 2,4-diisocyanate, diluted in acetone, was tested at concentrations up to 300 ug/plate with metabolic activation and up to 8 ug/plate without metabolic activation using the plate incorporation technique. **Toluene** 2,4-diisocyanate did not cause a positive response in any tester strain with or without metabolic activation.
[Haskell Laboratory; Mutagenic Activity of Toluene 2,4-Diisocyanate in the Salmonella/Microsome Assay, (1976), EPA Document No. FYI-OTS-0484-0302, Fiche No. OTS0000302-0] **UNREVIEWED**

Environmental Biodegradation :

Toluene diisocyanates are expected to be hydrolyzed much more rapidly than they are attacked by microorganisms. The resulting **toluene** diamines are subject to a wide variety of biochemical transformations. /**Toluene** diisocyanates/
[ITC/USEPA; Information Review #231 (Draft) Toluene Diisocyanates p.19 (1981)]**PEER REVIEWED**

Non-Human Toxicity Excerpts :

Groups of male and female rats and mice were exposed to 0.05 and 0.15 ppm of **toluene**-diisocyanate by inhalation for 6 hr/day, 5 days/week for approx 2 years. Type and incidence of tumors and the number of tumor-bearing animals of either species did not indicate any carcinogenic effect. Hematology, biochemistry, urinalysis, and cytogenicity did not reveal any untoward effect. Increased mortality (females only), reduced weight gain and signs of irritation in the upper and lower respiratory tract resulted from exposure to **toluene** diisocyante in the mouse study with the highest incidence in the 0.15 ppm exposure level. Male and female rats of the 0.15 ppm group gained less weight during the first 12 weeks of the study. Histopathological examination in the rat study has not been completed, but no effect in the respiratory tract or in any other tissue has yet been seen. /**Toluene** diisocyanate/
[Loeser E; Toxicol Lett 15 (1): 71-81 (1983)]**PEER REVIEWED**

Human Toxicity Excerpts :

Resp health of 277 **toluene** diisocyanate workers was studied prospectively. Peak and 8-hr TWA concn were determined in over 200 samples. Smoking had a significant effect on spirometric tests and lung volumes. After adjustment for smoking, the 74 men in the high **toluene** diisocyanate exposure group had significantly larger declines in forced expiratory vol than the 149 men in the low exposure category. /**Toluene** diisocyanate/
[Diem JE et al; Am Rev Respir Dis 126 (3): 420-8 (1982)]**PEER REVIEWED**

Non-Human Toxicity Excerpts :

Two strains of guinea pigs were parenterally immunized with well-characterized diisocyanate-protein conjugates. Hapten-specific IgE antibodies were detected in the sera of English short-hair strain guinea pigs immunized with **toluene** diisocyanate-human serum albumin when the serum was analyzed by the 168 hr passive cutaneous anaphylaxis technique followed by iv challenge with a conjugate coupled to an unrelated carrier protein, transferrin. IgG1 antibodies and precipitating antibodies were demonstrated in Hartley strain guinea pigs immunized with the **toluene** diisocyanate-human serum albumin conjugate. It became apparent that immune responses of guinea pigs immunized with protein conjugates of bifunctional isocyanates were heterogeneous and involved multiple specificities for hapten, carrier protein, and new antigenic determinants. It was postulated that the complex nature of the immune response generated by diisocyanate cmpd in the guinea pig may also serve as an appropriate model of isocyanate-induced human sensitivity reactions, which are known to involve diverse immunologic and nonimmunologic mechanisms. /**Toluene** diisocyanate/
[Chen SE, Bernstein IL; J Allergy Clin Immunol 70 (5): 383-92 (1982)]**PEER REVIEWED**

Probable Routes of Human Exposure :

... Reported 42 accepted or established cases of **toluene** diisocyanate intoxication and 73 questionable or disputed cases, among workers in 14 plants in MA between 1957 and 1962. In 14 of the accepted cases the avg **toluene** diisocyanate vapor concn found in the workroom was about 0.03 ppm, with very few samples showing more than 0.05 ppm; in 11 cases the avg concn was 0.015 ppm; in 9 cases levels below 0.01 ppm were found; in the remainder measurements ... could not be made. All plants, where avg exposures exceeded 0.01 ppm (some exposure values were as high as 1.2 ppm), had workers with related resp illness, but no such illnesses were reported in plants where avg exposures were 0.007 ppm or lower. /**Toluene** diisocyanate/
[American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices. 5th ed. Cincinnati, OH:American Conference of Governmental Industrial Hygienists, 1986. 401]**PEER REVIEWED**

Human Toxicity Excerpts :

AFTER OCCUPATIONAL EXPOSURE, 112 PLANT WORKERS WERE TESTED BY INHALATION CHALLENGE WITH 0.005 PPM TO 0.02 PPM **TOLUENE** DIISOCYANATE. NO **TOLUENE** DIISOCYANATE INDUCED IMMUNOLOGIC CHANGES WERE NOTED WITH THE EXCEPTION OF 3 INDIVIDUALS WHO DEMONSTRATED SMALL POSITIVE WHEAL-&-ERYTHEMA REACTIONS. AIRWAYS OBSTRUCTION WAS ALSO NOTED. /**TOLUENE** DIISOCYANATE/
[BUTCHER BT ET AL; J ALLERGY CLIN IMMUNOL 58 (1 PART 1): 89-100 (1976)]**PEER REVIEWED**

Analytic Laboratory Methods :

NIOSH Method 5521. Analyte: 2,4-**Toluene** diisocyanate. Matrix: Air. Procedure: High performance liquid chromatography, electrochemical and ultra violet detection. For 2,4-**toluene** diisocyanate this method has an estimated detection limit of 0.1 ug diisocyanate/sample. The precision/RSD is not determined. Applicability: The working range is from 5 ug/cu m 2,4-**toluene** diisocyanate to more than 1 mg/cu m for 100 liter air samples. Interferences: Any substance which elutes with the ureas and absorbs ultraviolet light or is electroactive will interfere with the analysis.
[U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. 5521-1]**PEER REVIEWED**

Non-Human Toxicity Excerpts :

Single or repeated exposure to concn of 2,4-**toluene** diisocyanate ranging from 0.05-14 mg/cu m (0.007-2 ppm) for periods of up to 3 hr resulted in reductions in respiratory rate in Swiss

mice. The concn of **toluene** diisocyanate that caused a 50% decrease in the respiratory rate in mice was reported to be 3 mg/cu m (0.39 ppm); pulmonary injury was characterized principally by squamous metaplasia of the respiratory epithelium.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 306 (1986)]**PEER REVIEWED**

Non-Human Toxicity Excerpts :

Groups of 50 male and 50 female B6C3F1 mice, 12 wk of age, were admin 120 or 240 mg/kg body wt (males) or 120 mg/kg body wt (females) commercial-grade (86% 2,4 isomer; 14% 2,6 isomer) **toluene** diisocyanate in corn oil by gavage on five days per wk for 105 wk. The concn of **toluene** diisocyanate ... was equivalent to 36 or 72 mg/ml and 18 or 36 mg/ml. Groups of 50 male and 50 female mice received corn oil only and served as vehicle controls. ... No treatment-related tumor was seen in male mice. The survival rate in females was: 34/50 (68%) control, 43/50 (86%) low-dose and 33/50 (66%) high-dose animals. In females, hemangiomas (in the spleen and subcutaneous tissues) and hemangiosarcomas (in the liver, ovaries and peritoneum) occurred in 0/50 (0%) control, 1/50 (2%) low-dose and 5/50 (10%) high-dose animals, giving a statistically significant positive trend (p= 0.01, Cochran-Armitage trend test). The incidence of hepatocellular adenomas was also significantly incr in females: 2/50 (4%) control, 3/50 (6%) low-dose and 12/50 (24%) high-dose animals (p= 0.001, Cochran-Armitage trend test).
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 302 (1986)]**PEER REVIEWED**

Probable Routes of Human Exposure :

3 CASES OF ACUTE POISONING OF WORKERS BY **TOLUENE** DIISOCYANATE WERE OBSERVED DURING 5 YR AT A HOSPITAL IN PARIS. 1 CASE WAS FATAL, THE OTHER 2 PATIENTS SURVIVED. AFTER REVIEW OF LITERATURE, CIRCUMSTANCES ARE DESCRIBED UNDER WHICH THIS POISONING IS LIKELY TO OCCUR. /**TOLUENE** DIISOCYANATE/
[GERVAIS P ET AL; J EUR TOXICOL 6 (6): 320-3 (1973)]**PEER REVIEWED**

Other Environmental Concentrations :

Commercial **toluene** diisocyanate typically contains 80% 2,4-**toluene** diisocyanate(1). TDI monomer has been found in a urethane foam fabric coating in concn of < 200 ppm(1).
[(1) IARC Monograph on the Evaluation of the Carcinogenic Risk of Chemicals to Humans, Some Chemicals used in Plastics and Elastomers 39: 287-323 (1985)]**PEER REVIEWED**

Environmental Abiotic Degradation :

2,4-**Toluene** diisocyanate reacts readily with compounds containing active hydrogens, such as water, acids, and alcohols(2). Contact with bases may cause uncontrollable polymerization with rapid evolution of heat(2). Hydrolysis of one of the isocyanate groups to the amine will be followed by rapid reaction of the amine with an isocyanate group on another molecule leading to dimers, oligomers, and polymers unless the solution is very dilute(2). In one experiment the hydrolysis product yield was 20% diamine and 80% polyurea(3). When 50 ppm of **toluene** diisocyanate was added to a model river and seawater systems, the concn was 0.1 ppm or less at the end of 1 day(1).
[(1) Duff PB; pp 408-12 in: Polyurethane-New Paths to Progress Marketing Technology (1983) (2) IARC Monograph on the Evaluation of the Carcinogenic Risk of Chemicals to Humans, Some Chemicals used in Plastics and Elastomers 39: 287-323 (1985) (3) Sopach ED, Boltromeyuk LP; Gig Sanit 7: 10-13 (1974)]**PEER REVIEWED**

General Manufacturing Information :

DINITROTOLUENE IS DIRECTLY CARBONYLATED IN THE PRESENCE OF AN ALCOHOL-PRODUCING URETHANE THAT DECOMPOSES TO **TOLUENE** DIISOCYANATE AND THE ALCOHOL (THE ALCOHOL AND CARBON DIOXIDE CAN BE RECYCLED) IN A PROCESS BEING DEVELOPED BY MITSUBISHI CHEMICAL CO. /**TOLUENE** DIISOCYANATE/
[CHEMICAL PRODUCTS SYNOPSIS: TOLUENE DIISOCYANATE, 1985]**PEER REVIEWED**

General Manufacturing Information :

Diisocyanates used in the polyurethane industry pose a possible threat to workers exposed to them. A method for generating low concn was developed using tetrafluoroethylene Teflon permeation tubes. The tubes were prepared by sealing in clean spaghetti tubing with solid tetrafluoroethylene Teflon rod held in place with crimped aluminum Swagelok ferrules. Using a commercially avail air bath capable of maintaining a temp within 0.05 deg K, the permeation tubes were kept at 303, 323 and 343 deg K **toluene** diisocyanate was swept from the thermostated chamber with dry nitrogen and further diluted with clean dry air to the desired concn. Permeation rates for the thick wall tube were 2.14 ng/min/cm at 303 deg K, 10.66 at 323 deg K and 42.84 at 343 deg K. For the thin wall tube, the permeation rates were 8.30 ng/min/cm at 303 deg K, 45.39 at 323 deg K and 179.62 at 343 deg K. /**Toluene** diisocyanate/
[Burg WR, Chang SN; Am Ind Hyg Assoc J 42 (6): 426-30 (1981)]**PEER REVIEWED**

Absorption, Distribution & Excretion :

Toluene diisocyanate may be absorbed into the body by inhalation, ingestion and through the skin. /**Toluene** diisocyanate/
[Handling Chemicals Safely 1980; 2nd Ed, Dutch Association of Safety Experts, the Dutch Chemical Industry Association and the Dutch Institute: 970]**PEER REVIEWED**

Human Toxicity Excerpts :

Several studies on the prognosis of isocyanate induced asthma show that a significant proportion of patients continue to experience asthmatic symptoms and nonspecific bronchial hyperresponsiveness after cessation of work, and that further exposure to isocyanates in sensitized subjects leads almost invariably to persistence of respiratory symptoms and of bronchial hyperresponsiveness and the deterioration of airway function. Specific bronchial reactivity to isocyanates may change after cessation of work; however, some subjects continue to be sensitive to **toluene** diisocyanate several months after cessation of work. The determination of an unfavorable prognosis for asthma seem to be the same as those for other types of occupational asthma due to low molecular weight compounds (ie red cedar asthma); long duration of exposure before the onset of asthma, long duration of symptoms before diagnosis, airway obstruction, and dual airway response after specific challenge tests. Also, single acute exposure to high levels of TDI in the workplace (spills) can result in persistent nonspecific bronchial hyperresponsiveness. Potential mechanisms of persistence of symptoms and of nonspecific bronchial hyperresponsiveness may be chronic inflammation, bronchial smooth muscle alteration, autonomic nervous system disregulation. /**Toluene** diisocyanate/
[Paggiaro PL et al; Bull Eur Physiophol Respir 23 (6): 565-9 (1987)]**PEER REVIEWED**

Non-Human Toxicity Excerpts :

Twenty-seven chemicals (including **toluene** 2,4-diisocyanate) previously tested in rodent carcinogenicity assays were tested for induction of chromosomal aberrations and sister chromatid exchanges in Chinese hamster ovary cells as part of a larger analysis of the correlation between results of in vitro genetic toxicity assays and carcinogenicity bioassays. Chemicals were tested up to toxic doses with and without exogenous metabolic activation. **Toluene** 2,4-diisocyanate at 300-1000 ug/ml did not induce chromosomal aberrations either with or without S9. Results from sister chromatid exchange assays were equivocal because, although no evidence for induction of sister chromatid exchanges was seen in tests conducted with S9, 2 of 3 trials performed in the absence of S9 and with delayed harvest showed a

significant elevation in the incidence of sister chromatid exchanges. In one trial, doses of 300-500 ug/ml resulted in a slight but significant rise in the number of sister chromatid exchanges per cell, but this response did not increase with dose; in the other, a significant dose related increase in the frequency of sister chromatid exchanges was observed within a range of 250-400 ug/ml.
[Gulati DK et al; Environ Mol Mutagen 13 (2): 133-93 (1989)]**PEER REVIEWED**

Human Toxicity Excerpts :

Neurological symptoms were reported in 23 firemen heavily exposed to **toluene** diisocyanate during a polyurethane manufacturing plant fire. Symptom included euphoria, ataxia, and loss of consciousness with long lasting mild subjective symptoms of personality change, irritability, depression, and memory difficulties. /**Toluene** diisocyanate/
[O'Donoghue, J.L. (ed.). Neurotoxicity of Industrial and Commercial Chemicals. Volume II. Boca Raton, FL: CRC Press, Inc., 1985. 34]**PEER REVIEWED**

Threshold Limit Values :

Notice of Intended Change (first notice appeared in 1998 edition): The ACGIH has listed chemicals for which either a limit has been proposed for the first time, for which a change in the "Adopted" listing has been proposed, or for which retention on the Notice of Intended Changes has been proposed. The proposed limits should be considered trial limits that will remain in the listing for a period of at least one year. If, after one year no evidence comes to light that questions the appropriateness of the values herein, the values will be reconsidered for the "Adopted" list. Time Weighted Avg (TWA):0.005 ppm; Short Term Exposure Limit (STEL): 0.02 ppm. /**Toluene**-2,4-diisocyanate or **toluene**-2,6-diisocyanate (or as mixture)/
[American Conference of Governmental Industrial Hygienists. TLVs and BEIs. Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. Cincinnati, OH. 2000. 76]**QC REVIEWED**

Sampling Procedures :

NIOSH Method 5521. Analyte: 2,4-**Toluene** diisocyanate. Matrix: Air. Sampler: Impinger (solution of 1-(2-methoxyphenyl)-piperazine in **toluene**). Flow Rate: 1 l/min: Sample Size: 100 liters. Shipment: Ship in screw-cap vial refrigerated @ 4 deg C or lower. Sample Stability: May be unstable.
[U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. 5521-1]**PEER REVIEWED**

Human Toxicity Excerpts :

Toluene diisocyanate may produce a true hemorrhagic syndrome affecting the bone marrow and producing primarily thrombocyte series suppression. /**Toluene** diisocyanate/
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 303]**PEER REVIEWED**

Human Toxicity Excerpts :

Highly reactive low molecular weight cmpd such as **toluene** diisocyanate, used in a variety of chem processes, paints and plastics, are replacing the more classical protein antigens as the most commonly implicated agents in occupational asthma. /**Toluene** diisocyanate/
[Ullrich IH; W Va Med J 78 (6): 140-4 (1982)]**PEER REVIEWED**

Human Toxicity Excerpts :

SOME WORKERS BECOME EXCEEDINGLY SENSITIVE TO **TOLUENE**

DIISOCYANATE VAPORS & RESPOND DRAMATICALLY TO MINUTE AMT OF THIS MATERIAL IN THE AIR. /**TOLUENE** DIISOCYANATE/
[Hamilton, A., and H. L. Hardy. Industrial Toxicology. 3rd ed. Acton, Mass.: Publishing Sciences Group, Inc., 1974. 336]**PEER REVIEWED**

Analytic Laboratory Methods :

LIQ CHROMATOGRAPHY HAS BEEN USED TO SEPARATE **TOLUENE** DIISOCYANATE ISOMERS AS UREA DERIVATIVES FROM PREPD MIXT ... WITH DETECTION BY UV SPECTROSCOPY. LIMIT OF DETECTION WAS 1.2 NG OF 2,4- OR 2,6-ISOMER. GAS CHROMATOGRAPHY WITH ELECTRON CAPTURE DETECTION HAS BEEN USED TO DETERMINE 2,4-**TOLUENE** DIISOCYANATE IN ... AIR, WITH LOWER LIMIT OF DETECTION OF 0.035 MG/CU M (0.005 PPM).
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V19 309 (1979)]**PEER REVIEWED**

Human Toxicity Excerpts :

The report of a 5 yr follow-up study of 107 workers in a polyurethane manufacturing plant using forced expiratory vol measurements and questionnaires on resp symptoms and smoking habits is presented. **Toluene** diisocyanate exposure levels were monitored. Mean forced expiratory vol was higher than that predicted for healthy subjects and the 5 yr change in forced expiratory vol did not exceed that expected from aging. No acute changes in forced expiratory vol was observed on a Monday either before or after a 2 wk vacation and no ventilatory function improvement was observed during vacation. Low-level isocyanate exposure (time-weighted avg concn around 0.001 ppm) was not assoc with chronic resp symptoms or effects on ventilatory capacity. /**Toluene** diisocyanate/
[Musk AW et al; J Occup Med 24 (10): 746-50 (1982)]**PEER REVIEWED**

Artificial Pollution Sources :

2,4-**Toluene** diisocyanate may be released to the environment, primarily as stack and fugitive emissions into air during its commercial production, handling, and processing prior to polyurethane foam production(1). It may also be released during the manufacture of polyurethane foam products and coatings, from sprays, insulation materials, and polyurethane foam coated fabrics(1). About 0.005% of the **toluene** diisocyanate (TDI) used in flexible foam slabstock plants is released in vent stack exhaust and this contains < 50% of the 2,4-isomer(2). Large quantities of TDI are transported by rail, road, and sea and there is a possibility of spills during loading or unloading(2).
[(1) IARC Monograph on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Some Chemicals used in Plastics and Elastomers, 39: 287-323 (1985) (2) Brochhagen FK, Grieveson BM; Cellular Polymers 3: 11-17 (1984)]**PEER REVIEWED**

Analytic Laboratory Methods :

NIOSH Method 2535. Analyte: **Toluene**-2,4-diisocyanate. Matrix: Air. Procedure: High performance liquid chromatography, ultra violet detection. For 2,4-**toluene** diisocyanate this method has an estimated detection limit of 0.1 ug/sample. The precision/RSD is 0.067 and the recovery is 2 ml methanol, ultrasonic bath 3 min. Applicability: The working range is 0.1004 to 0.35 ppm (0.03 to 2.5 mg/cu m) for a 10-liter air sample. Interferences: The reagent is slightly unstable in the dark at 25 deg C. Tailing during high performance liquid chromatography, a result of reagent deterioration, may raise detection limit.
[U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office,

February 1984.,p. 2535-1]**PEER REVIEWED**

Human Toxicity Excerpts :

20 CASES OF OCCUPATIONAL /SKIN CONDITIONS/ CAUSED BY ISOCYANATES ESP **TOLUENE** DIISOCYANATE ARE REPORTED. FINDINGS GIVE SOME EVIDENCE FOR CROSS-SENSITIZATION BETWEEN CHEMICALLY RELATED CMPD. /**TOLUENE** DIISOCYANATE/
[ROTHE A; BERUFSDERMATOSEN 24 (1): 7-24 (1976)]**PEER REVIEWED**

Mechanism of Action :

Exposure of workers to isocyanates may result in irritation and/or sensitization of the resp tract. An immunologic mechanism for sensitization has been presented. This investigation explored whether, as a possible mechanism for the irritation reaction, the toxic resp effect of isocyanates might be due to their ability to inhibit cholinesterase. Molar ratios of 50:1 or greater were required for 50% inhibition of purified human serum cholinesterase by 2,4-**toluene** diisocyanate. When whole human plasma was the source of cholinesterase, the molar concn of 2,4-**toluene** diisocyanate needed to effect 50% enzyme inhibition suggested affinity labeling by this reagent.
[Brown WE et al; Toxicol Appl Pharmacol 63 (1): 45-52 (1982)]**PEER REVIEWED**

Human Toxicity Excerpts :

In 37 polyurethane workers with isocyanate asthma, exam carried out 40 mo after exposure had ceased showed that asthmatic symptoms had disappeared in 32 workers but that chronic bronchitis had developed in six. The progressive impairment of ventilatory function was evaluated by measuring the decr in forced vital capacity and forced expiratory vol after exposure had ceased. Mean annual decr of 86.3 and 67.7 ml, respectively, were observed. **Toluene** diisocyanate induces chronic and irreversible lung damage even after exposure is discontinued, and impairment of forced vital capacity is greater than that of forced expiratory volume. /**Toluene** diisocyanate/
[Innocenti A et al; Medicina del Lavoro 72 (3): 231-7 (1981)]**PEER REVIEWED**

Non-Human Toxicity Excerpts :

Groups of 50 male and 50 female Fischer 344/N rats, 11 wk old, were admin 30 or 60 mg/kg body wt (males) or 60 or 120 mg/kg body wt (females) commercial-grade **toluene** diisocyanate (86% 2,4 isomer; 14% 2,6 isomer) in corn oil by gavage on five days per wk for 106 wk. The concn of **toluene** diisocyanate was 9 or 18 mg/ml and 18 or 36 mg/ml. Groups of 50 male and 50 female rats received corn oil only and served as vehicle controls. ... A treatment-related incr in the incidence of subcutaneous fibromas and fibrosarcomas individually and combined was observed in males. The incidence of fibrosarcomas was 0/50 control, 3/50 low-dose and 3/50 high-dose animals; the combined incidence was 3/50 (6%) control, 6/50 (12%) low-dose and 12/50 (24%) high-dose animals. ... The overall rate of mammary fibroadenomas in female rats was: 15/50 (30%) controls, 21/50 (42%)low-dose and 18/50 (36%) high-dose. ... The terminal tumor rate for mammary fibroadenomas was: 13/36 (36%) controls, 15/19 (79%) low-dose and 4/6 (67%) high-dose animals. The dose-related incidence of pancreatic acinar-cell adenomas in males ... was significantly incr in the high-dose compared to controls (p= 0.034). In females, pancreatic islet-cell adenomas were found at terminal sacrifice in 0/36 controls, 3/19 low-dose and 2/6 high-dose animals (p is less than or equal to 0.01, tests for incidental tumors comparing each dose group to controls). One islet-cell carcinoma was observed in one low-dose female. A dose-related increase in the incidence of neoplastic nodules in the liver of female rats was also noted.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 303 (1986)]**PEER REVIEWED**

Human Toxicity Excerpts :

FIREMEN EXPOSED TO FUMES OF **TOLUENE** DIISOCYANATE EXPERIENCED SYMPTOMS DURING & AFTER FIRE. SYMPTOMS WERE MAINLY GI, RESP, OR NEUROLOGICAL. GI SYMPTOMS SUBSIDED WITHIN 2 DAYS OF ONSET, SOME MEN SUSTAINED LONG-TERM RESP TRACT DAMAGE. /**TOLUENE** DIISOCYANATE/
[AXFORD AT ET AL; BR J IND MED 33 (2): 65-71 (1976)]**PEER REVIEWED**

Human Toxicity Excerpts :

... **Toluene** diisocyanate is an irritant causing inflammation and occasional sensitization of skin, lacrimation, smarting, burning, and pricking sensation in the eyes; abdominal distress, nausea, and vomiting. ... Exposure to high concn may lead to chemical bronchitis with severe bronchospasm, chemical pneumonitis, pulmonary edema, headache, and insomnia. ... Repeated exposure at lower concn may produce a chronic-like syndrome in many people. Symptoms may incl coughing, wheezing, tightness, or congestion in the chest and shortness of breath. ... /**Toluene** diisocyanate/
[American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices. 5th ed. Cincinnati, OH:American Conference of Governmental Industrial Hygienists, 1986. 580]**PEER REVIEWED**

Human Toxicity Excerpts :

AS A VAPOR **TOLUENE** DIISOCYANATE IS A POWERFUL IRRITANT TO ... RESPIRATORY TRACT. INDUSTRIAL EXPOSURES TO SURPRISINGLY LOW CONCN HAVE PRODUCED RESPIRATORY SYMPTOMS: A SENSATION OF CONSTRICTION OF CHEST, COUGH & DYSPNEA. SIMILARITY TO ASTHMATIC ATTACK WITH SEVERE BRONCHOSPASM HAS BEEN MENTIONED ... X-RAYS WERE UNIFORMLY NEGATIVE. EOSINOPHILIA WAS NOTED. REMOVAL FROM EXPOSURE HAS RESULTED IN SEQUELAE-FREE RECOVERY, BUT ON RE-EXPOSURE THERE MAY BE INCREASED SENSITIVITY. /**TOLUENE** DIISOCYANATE/
[Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984.,p. II-414]**PEER REVIEWED**

Disposal Methods :

Toluene diisocyanate is a waste chemical stream constituent which may be subjected to ultimate disposal by controlled incineration. Controlled incineration: Oxides of nitrogen are removed from the effluent gas by scrubbers and/or thermal devices. /**Toluene** diisocyanate/
[USEPA; Engineering Handbook for Hazardous Waste Incineration p.2-10 (1981) EPA 68-03-3025]**PEER REVIEWED**

Preventive Measures :

Because pulmonary effects can be produced in man at very low levels in air, **toluene** diisocyanate should be used only in areas with adequate general and local ventilation ... . /**Toluene** diisocyanate/
[Clayton, G. D. and F. E. Clayton (eds.). Patty's Industrial Hygiene and Toxicology: Volume 2A, 2B, 2C: Toxicology. 3rd ed. New York: John Wiley Sons, 1981-1982. 4893]**PEER REVIEWED**

Preventive Measures :

APPROPRIATE PROTECTIVE MEASURES FOR WORKERS WITH ... /**TOLUENE** DIISOCYANATE/ PRESENT A MAJOR DIFFICULTY, SINCE CONCENTRATIONS OF THE CHEMICAL AS LOW AS 0.01 PPM ARE APPARENTLY TOO HIGH FOR SAFETY. /**TOLUENE** DIISOCYANATE/
[Arena, J. M. Poisoning: Toxicology, Symptoms, Treatments. Fourth Edition. Springfield, Illinois: Charles C. Thomas, Publisher, 1979. 226]**PEER REVIEWED**

Skin, Eye and Respiratory Irritations :

AS A VAPOR ... /**TOLUENE** DIISOCYANATE/ IS A POWERFUL IRRITANT TO EYES, SKIN, RESPIRATORY TRACT. /**TOLUENE** DIISOCYANATE/
[Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984.,p. II-414]**PEER REVIEWED**

General Manufacturing Information :

... MANY /SPANDEX FORMULATIONS/ ARE BASED ON ... 2,4-**TOLUENE** DIISOCYANATE. ...
[Hamilton, A., and H. L. Hardy. Industrial Toxicology. 3rd ed. Acton, Mass.: Publishing Sciences Group, Inc., 1974. 347]**PEER REVIEWED**

Methods of Manufacturing :

Usually prepared from **toluene**-2,4-diamine and phosgene.
[Budavari, S. (ed.). The Merck Index - Encyclopedia of Chemicals, Drugs and Biologicals. Rahway, NJ: Merck and Co., Inc., 1989. 1501]**PEER REVIEWED**

Methods of Manufacturing :

NITRATION OF **TOLUENE**, FOLLOWED BY REDUCTION TO DIAMINE, REACTION WITH PHOSGENE, PURIFICATION, AND RECOVERY OF COPRODUCT HYDROGEN CHLORIDE.
[CHEM & ENG NEWS 63 (37): 16 (1985)]**PEER REVIEWED**

Synonyms :

TOLUENE, 2,4-DIISOCYANATO-
PEER REVIEWED

Synonyms :

TOLUENE-2,4-DIISOCYANATE
PEER REVIEWED

Synonyms :

META-**TOLUENE** DIISOCYANATE
PEER REVIEWED

Human Toxicity Excerpts :

ACCIDENTAL SPLASH ... IN EYES OF WORKMEN HAS CAUSED KERATITIS & CONJUNCTIVITIS. ONE CASE ... DESCRIBES "UNUSUAL AMT OF PHOTOPHOBIA & BLEPHAROSPASM" ... SECOND CASE ... DESCRIBED ... INVOLVED SEVERE IRIDOCYCLITIS & SECONDARY GLAUCOMA. /**TOLUENE** DIISOCYANATE/
[Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986. 929]**PEER REVIEWED**

Human Toxicity Excerpts :

AN IMMUNOLOGIC TEST PROCEDURE WAS USED ON WORKERS IN A **TOLUENE** 2,4-DIISOCYANATE PLANT. IMMUNOLOGIC CHANGES PRODUCING TOLERANCE TO TDI EXPOSURE ALSO RESULTED IN NEGATIVE RESPONSE TO ANTIGEN CHALLENGE TESTS. SOME INDIVIDUALS EXPOSED TO TDI MAY HAVE PROTECTIVE ANTIBODIES BUT STILL EXPERIENCE BRONCHOCONSTRICTION.
[PORTER CV ET AL; AM IND HYG ASSOC J 36 (3): 159-68 (1975)]**PEER REVIEWED**

Special Reports :

TSCA CHIPs present a preliminary assessment of **toluene** 2,4-diisocyanate's potential for injury to human health & the environment (available at EPA's TSCA Assistance Office: (202)

554-1404

Sampling Procedures :

NIOSH Method 2535. Analyte: **Toluene**-2,4-diisocyanate. Matrix: Air. Sampler: Tube with reagent coated glass wool (N-((4-nitrophenyl) methyl)-propylamine on glass wool). Flow Rate: 0.2 to 1 l/min: Sample Size: 10 liter. Shipment: Protect from light. Sample Stability: At least 14 days at 25 deg C.
[U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. 2535-1]**PEER REVIEWED**

FDA Requirements :

Toluene 2,4-diisocyanate is an indirect food additive for use only as a component of adhesives.
[21 CFR 175.105 (4/1/91)]**PEER REVIEWED**

RCRA Requirements :

U223; As stipulated in 40 CFR 261.33, when **toluene**-2,4-diisocyanate as a commercial chemical product or manufacturing chemical intermediate or an off-specification commercial chemical product or a manufacturing chemical intermediate, becomes a waste, it must be managed according to Federal and/or State hazardous waste regulations. Also defined as a hazardous waste is any residue, contaminated soil, water, or other debris resulting from the cleanup of a spill, into water or on dry land, of this waste. Generators of small quantities of this waste may qualify for partial exclusion from hazardous waste regulations (40 CFR 261.5).
[40 CFR 261.33 (7/1/91)]**PEER REVIEWED**

Atmospheric Standards :

This action promulgates standards of performance for equipment leaks of Volatile Organic Compounds (VOC) in the Synthetic Organic Chemical Manufacturing Industry (SOCMI). The intended effect of these standards is to require all newly constructed, modified, and reconstructed SOCMI process units to use the best demonstrated system of continuous emission reduction for equipment leaks of VOC, considering costs, non air quality health and environmental impact and energy requirements. **Toluene**-2,4-diisocyanate is produced, as an intermediate or a final product, by process units covered under this subpart.
[40 CFR 60.489 (7/1/91)]**PEER REVIEWED**

Probable Routes of Human Exposure :

Pulmonary function tests were done and compared to current and past potential exposure levels of **toluene** diisocyanate (TDI) for 57 TDI manufacturing workers and 89 workers not exposed to TDI or other known respiratory hazards. The avg TDI plant experience at Texas Operations of Dow Chemical USA was 4.1 + or - 2.8 yr. Routine industrial hygiene measurements have shown TDI exposure below a time weighted avg of 0.005 ppm and a short term exposure of 0.02 ppm. Ranking was made of department and job classification by level of potential exposure to TDI (none, n= 10; moderate, n= 14; and high, n= 33). TDI exposure, whether classified as current, highest career level, cumulative or cumulative highest to date, was not associated with a decline of forced expiratory volume.
[Olsen GW et al; J Occup Med 31 (8): 664-7 (1989)]**PEER REVIEWED**

Effluent Concentrations :

Toluene diisocyanate (TDI), no isomer specified, has been reported in waste water from furniture manufacturing in the concn range of 0.1- 4.1ppm(1). Stack exhaust from a polyurethane foam production plant were reported to contain 100-17,700 ug/cu m of TDI (no isomer specified)(1).
[(1) IARC Monograph on the Evaluation of the Carcinogenic Risk of Chemicals to Humans, Some Chemicals used in Plastics and

Elastomers 39: 287-323 (1985)]**PEER REVIEWED**

Volatilization from Water/Soil :

The vapor pressure of 2,4-**toluene** diisocyanate is 0.01 torr at 20 deg C(1) and, therefore, spilled TDI will not readily volatilize from soil and surfaces(SRC).
[(1) IARC Monograph on the Evaluation of the Carcinogenic Risk of Chemicals to Humans, Some Chemicals used in Plastics and Elastomers 39: 287-323 (1985)]**PEER REVIEWED**

Environmental Abiotic Degradation :

Gas phase loss of TDI was originally thought to be due to reaction of TDI with water vapor(2). One early work showed that the percent disappearance of TDI in air depended almost solely on the water vapor concentration, increasing 3.2% per unit increase in absolute humidity (g water/kg dry air), so that at 15 g water/kg dry air, a 50% reduction in TDI was obtained(2). These reductions were obtained after 8 sec and did not differ appreciably after 75 sec(2). The reaction product of 2,4-**toluene** diisocyanate vapor with limited quantities of moisture was reported to be 3,3'-diisocyanto-4,4'-dimethylcarbanilide(1). Other work contradicted these earlier findings and a program was instituted to study the gas-phase reactions between TDI and water using a room sized environmental chamber(4). They found that over a relative humidity range of 7-70%, the loss rate of TDI was independent of humidity and no toluenediamine or TDI-urea products could be detected(4). In addition deposition onto the chamber walls was an important removal process(4). Subsequent experiments were performed in the environmental chamber to assess the importance of photolysis, reaction with free radicals, and adsorption onto particulate matter as atmospheric removal processes(3). The loss rate of TDI in irradiated clean air was first order with a half-life of 3.3 hr(3). By using a free radical scavenger, it was shown that free-radicals and not photolysis was responsible for the removal. The half-life is consistent with the reaction with photochemically generated hydroxyl radicals(3). The addition of an urban surrogate hydrocarbon mixture (polluted urban air) or ammonium sulfate particulate matter, a major component of atmospheric aerosols, did not significantly alter removal rates(3). Because the concentration of hydroxyl radicals generally increases in polluted air, shorter half-lives are expected(SRC).
[(1) Marcali K; Anal Chem 29: 552 (1957) (2) Dyson WL, Hermann ER; Amer Ind Hyg Assoc J 32: 741-4 (1971) (3) Duff PB; Proc of the SPI Tech/Mark Conf 29: 9-14 (1985) (4) Duff PB; pp 408-12 in: Polyurethane-New Paths to Progress Marketing Technology (1983)]**PEER REVIEWED**

Mechanism of Action :

... The sensitizing agent /such as **toluene** diisocyanate/ acts in vivo to haptenate self-proteins, and this haptenated self-protein serves as the stimulus for generation of the allergic immune response.
[Doull, J., C.D.Klassen, and M.D. Amdur (eds.). Casarett and Doull's Toxicology. 3rd ed., New York: Macmillan Co., Inc., 1986. 265]**PEER REVIEWED**

Special Reports :

NIOSH; Current Intelligence Bulletin 53. **Toluene** Diisocyanate (TDI) and Toluenediamine (TDA): Evidence of Carcinogenicity. (1989)

Non-Human Toxicity Excerpts :

Groups of 120 male and 120 female CD-1 mice, three to four weeks old, were exposed to 0, 0.05 or 0.15 ppm (0, 0.36 or 1.07 mg/cu m) production-grade **toluene** diisocyanate (approx 80% 2,4 isomer & 20% 2,6 isomer) in an inhalation chamber for 6 hr/day on 5 days/wk for 104 wk. There was a significant reduction in body weight in the high-dose group (sex not stated) and a significant increase in mortality in both high- and low-dose females by the termination of the study. No such effect was seen in males. Neither the types of tumors observed nor their incidences were dose-related, and both corresponded to those seen in historical controls for this strain of mice. However, dose-related pathological changes were observed in the nasal cavity

(chronic or necrotic rhinitis), together with changes in the lower respiratory tract (interstitial pneumonia, catarrhal bronchitis) in both groups.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 303 (1986)]**PEER REVIEWED**

CERCLA Reportable Quantities :

Releases of CERCLA hazardous substances are subject to the release reporting requirement of CERCLA section 103, codified at 40 CFR part 302, in addition to the requirements of 40 CFR part 355. **Toluene** 2,4-diisocyanate is an extremely hazardous substance (EHS) subject to reporting requirements when stored in amounts in excess of its threshold planning quantity (TPQ) of 500 lbs.
[40 CFR 355 (7/1/97)]**QC REVIEWED**

Atmospheric Standards :

Listed as a hazardous air pollutant (HAP) generally known or suspected to cause serious health problems. The Clean Air Act, as amended in 1990, directs EPA to set standards requiring major sources to sharply reduce routine emissions of toxic pollutants. EPA is required to establish and phase in specific performance based standards for all air emission sources that emit one or more of the listed pollutants. 2,4-**Toluene** diisocyanate is included on this list.
[Clean Air Act as amended in 1990, Sect. 112 (b) (1) Public Law 101-549 Nov. 15, 1990]**QC REVIEWED**

NIOSH Recommendations :

NIOSH considers **toluene**-2,4-diisocyanate to be a potential occupational carcinogen.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 312]**QC REVIEWED**

Probable Routes of Human Exposure :

Exposure to 2,4-**toluene** diisocyanate is primarily occupational via inhalation contact with aerosol or vapor. Dermal exposure occurs through skin contact with freshly cured foam or as a result of spills or splashes. (SRC)
PEER REVIEWED

Natural Pollution Sources :

2,4-**Toluene** diisocyanate is not known to occur as a natural product(1).
[(1) IARC Monograph on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Some Monomers, Plastics and Synthetic Elastomers, and Acrolein 19: 303-11 (1979)]**PEER REVIEWED**

Mechanism of Action :

EXPOSURE TO **TOLUENE** 2,4-DIISOCYANATE RESULTED IN DECR OF CO-DIFFUSION CONSTANT, WHICH GAVE RISE TO DIFFUSE INTERSTITIAL PULMONARY FIBROSIS. THESE EFFECTS WERE OBSERVED IN WORKERS IN FOAM MFR FOR AUTOMOBILE SEATS.
[PHAM QT ET AL; ANN OCCUP HYG 21 (3): 271-5 (1978)]**PEER REVIEWED**

Mechanism of Action :

It ... has been reported that **toluene** diisocyanate forms antigenic complexes with proteins, transforms lymphocytes in sensitized individuals, induces skin-sensitizing antibodies in animals, and induces specific antibody formation.
[Haddad, L.M. and Winchester, J.F. Clinical Management of Poisoning and Drug Overdosage. Philadelphia, PA: W.B. Saunders Co., 1983. 798]**PEER REVIEWED**

Absorption, Distribution & Excretion :

The absorption of gases in the respiratory tract is discussed. Formulas are presented for calculating saturation vapor concentrations and diffusion coefficients of gas absorption by the respiratory tract. Values are listed for 51 gases and vapors. Examples of the behavior of inhaled vapor and gaseous contaminants are ... **toluene**-2,4-diisocyanate. Foreign gases contaminating inhaled air are absorbed in the respiratory tract by diffusion of the gas molecules to the surface of the airways. No gas can penetrate beyond the lungs or enter the alveolar region if contaminant molecules are eliminated. Elimination at the wall depends on the solubility of the gas molecules or on chemical fixation. In high concentrations, some gases can saturate the surfaces of the dead space airways. This action can stop diffusion, and penetration of the alveoli then takes place.
[Davies CN; Annals of Occup Hyg 29 (1): 13-25 (1985)]**PEER REVIEWED**

Non-Human Toxicity Excerpts :

Groups of 126 male and 126 female Sprague-Dawley CD rats, six to nine weeks old, were exposed to 0, 0.05 or 0.15 ppm (0, 0.36 or 1.07 mg/cu m) production-grade **toluene** diisocyanate (approx 80% 2,4 isomer and 20% 2,6 isomer) in an inhalation chamber for 6 hr/day on 5 days/wk for 108 wk or 110 wk. A significant reduction in weight gain was observed during the first 12 wk of the study among the high-dose animals of each sex, but body-weight gain was similar in all groups thereafter. No significant difference in mortality between treated and control groups of either sex was reported. Tumor incidences and types were reported to be similar in control and treated groups.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 304 (1986)]**PEER REVIEWED**

Non-Human Toxicity Excerpts :

Lesions occurring in the resp tract of mice after exposure to 10 sensory irritants, at a concn which elicited a resp rate decr of 50%, were compared with respect to type and severity. The RD50 of 2,4-**toluene** diisocyanate was 0.4 ppm. After exposure of mice for 6 hr/day for 5 days, the resp tract was examined for histopathological changes. All irritants produced lesions in the nasal cavity with a distinct anterior-posterior severity gradient.
[Buckley LA et al; Toxicol Appl Pharmacol 74 (3): 417-29 (1984)]**PEER REVIEWED**

Human Toxicity Excerpts :

A 46 year old man who had worked in a paint processing plant for over 29 years was admitted to the hospital with complaints of nocturnal dyspnea and dry cough. A chest X-ray film showed diffuse granular shadows in bilateral lungs. Pulmonary function tests revealed reduction of diffusing capacity and restrictive impairments. Hypersensitivity pneumonities due to isocyanates was speculated from his occupational history and clinical course. Positive skin tests against TDT-HSA and MDI-HSA, precipitating antibody against TDI-HSA, and negative lymphocyte stimulating tests of peripheral blood and bronchoalveolar lavage fluid were also noticed. Environmental provocation test was positive. Histological findings of transbronchial lung biopsy specimens showed diffuse alveolitis and Masson body, but no granulomas. According to these results, the patient was diagnosed as hypersensitivity pneumonitis due to **toluene** diisocyanate. Type III allergy of Gell-Coomhbs seems to participate in this case. The granulomatous lesion is seen less frequently in isocyanate-related hypersensitivity pneumonitis than in hypersensitivity pneumonitis induced by organic dusts, which suggest the difference in immunological and histological reactions between both types of hypersensitivity pneumonitis.
[Nozawa S et al; Nippon Kyobu Shikkan Gakkai Zasshi 27 (11): 1335-41 (1989)]**PEER REVIEWED**

Human Toxicity Excerpts :

Clinical signs of isocyanate exposure involved mucosal irritation of the respiratory and gastrointestinal tracts. Conjunctival irritation, skin inflammation (erythema, pain, vesiculation),

and gastrointestinal disturbances (nausea, vomiting, abdominal pain) occur soon after exposure. Pulmonary symptoms include cough, burning, substernal pain, dyspnea, choking sensation, sputum production, and hoarseness. Prominent bronchospasm (eg, wheezing, rhonchi, dyspnea, cough) may be present. Neurologic symptoms include headache, insomnia, euphoria, ataxia, anxiety neurosis, depression, and paranoia which may persist for several weeks. Persistent memory deficits, personality changes, irritability, and depression have been reported after severe exposures to **toluene** diisocyanate. Lacrimation, photophobia, profuse lid edema, and superficial corneal abrasions were the most common ophthalmologic effects at Bhopal. No case of blindness or irreversible ocular damage was noted on follow-up examination. /Isocyanates/
[Ellenhorn, M.J. and D.G. Barceloux. Medical Toxicology - Diagnosis and Treatment of Human Poisoning. New York, NY: Elsevier Science Publishing Co., Inc. 1988. 881]**PEER REVIEWED**

Human Toxicity Excerpts :

Strong mucous membrane irritation causes eye, pulmonary, and gastrointestinal tract symptoms. These compounds are potent pulmonary sensitizers which cause bronchospasm, even in patients without prior airway hyperreactivity. Diisocyanate compounds act either as inducers of nonspecific bronchial hyperreactivity or as direct pharmacologic agonists. Isocyanates apparently have the potential to sensitize certain segments of the population. Elevated humoral antibodies (ie, specific IgE antibodies to the p-tolyl determinant but not the diisocyanate conjugate) were detected in sensitized workers, but cell-mediated immunity also may produce hypersensitivity reactions. In the absence of renewed exposure, radioallergosorbent titers may not distinguish sensitive from nonsensitized workers. At high doses, **toluene** diisocyanate may act directly on bronchial mucosa by interfering with cholinergic and adrenergic mechanisms. /Isocyanates/
[Ellenhorn, M.J. and D.G. Barceloux. Medical Toxicology - Diagnosis and Treatment of Human Poisoning. New York, NY: Elsevier Science Publishing Co., Inc. 1988. 881]**PEER REVIEWED**

Human Toxicity Excerpts :

ORGANIC ISOCYANATES ARE PARTICULARLY POISONOUS WHEN BREATHED. FURTHERMORE THE TOXICITY VARIES ACCORDING TO PHYSICAL & CHEMICAL NATURE OF ISOCYANATE. AMONG MOST POISONOUS ... ARE **TOLUENE** 2,4- & 2,6-DIISOCYANATES.
[Lefaux, R. Practical Toxicology of Plastics. Cleveland: CRC Press Inc., 1968. 100]**PEER REVIEWED**

Sampling Procedures :

NIOSH Method 141. Analyte: 2,4-**toluene** diisocyanate. Matrix: Air. Procedure: Colorimetric. Flow Rate: 1 liter/min. Sample Size: 20 liters.
[U.S. Department of Health, Education Welfare, Public Health Service. Center for Disease Control, National Institute for Occupational Safety Health. NIOSH Manual ofAnalytical Methods. 2nd ed. Volumes 1-7. Washington, DC: U.S. Government Printing Office, 1977-present.,p. 141-1]**PEER REVIEWED**

Sampling Procedures :

A passive dosimeter for monitoring occupational exposure to both 2,6- and 2,4-**toluene** diisocyanate (TDI) was developed. The device is constructed from a 37 mm aerosol cassette. The collection medium used in the dosimeter is 0.5% sulfuric acid. Membranes of both the permeation and diffusion types were evaluated for use in the dosimeter. Microporous teflon diffusion membranes exhibited superior performance in terms of surface effects (mass transfer coefficient <0.006 ug/ppb/hr) and residual TDI (not detected) and were chosen for use. Collected TDI is determined as toluenediamine by either colorimetry using a modification of the Marcali technique or fluorometry using fluorescamine reagent. The manufacturer claims an accuracy of + or - 15%. A significant dependence on wind speed was minimized by use of a

second microporous membrane as a wind screen. The mass transfer rate of TDI was found to be approximately 0.0152 ug/ppb/hr and was equivalent for the 2,4- and 2,6- isomers of TDI.
[Rando RJ et al; Am Ind Hyg Assoc J 50 (1): 1-7 (1989)]**PEER REVIEWED**

Immediately Dangerous to Life or Health :

NIOSH considers **toluene**-2,4-diisocyanate to be a potential occupational carcinogen.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 312]**QC REVIEWED**

Environmental Fate :

TERRESTRIAL FATE: Ten days after a spill of 13 tons of **toluene** diisocyanate (TDI) onto swampy, wet forest soil, TDI and toluenediamines were found in the soil(1,2). The TDI solidified and the area was covered with sand. The soil concn of TDI and toluenediamine combined declined from the parts per thousand to parts per million range between 10 days and 12 wk after the spill(2). No TDI was detected in a connecting brook 10 days after the spill(2). After 6 years, only TDI-derived polyureas were found at the site(1). In a simulated spill, 5 kg of TDI in a container was covered with 50 kg of sand and 5 kg of water at ambient temperatures and samples taken from the top and bottom of the sand pile. After 24 hr, 5.5% of the TDI remained unreacted and after 8 days 3.5% remained(2). The reaction product was largely polyureas(2).
[(1) IARC Monograph on the Evaluation of Carcinogenic Risk of Chemicals to Humans. Some Chemicals used in Plastics and Elastomers. 39: 287-323 (1985) (2) Brochhagen FK, Grieveson BM; Cellular Polymers 3: 11-17 (1984)]**PEER REVIEWED**

Populations at Special Risk :

IN VIEW OF POTENTIALLY HAZARDOUS LEVELS OF **TOLUENE** DIISOCYANATE IN COMMERCIALLY AVAIL AEROSOLS, PRODUCTS SHOULD BE PROPERLY LABELED & PATIENT WITH ALLERGIC DIATHESES & OBSTRUCTIVE LUNG DISEASE CAUTIONED AGAINST THEIR USE.
[PETERS JM, MURPHY R LH; AM REV RESPIR DIS 104 (3): 432-3 (1971)]**PEER REVIEWED**

Non-Human Toxicity Excerpts :

2,4-**Toluene** diisocyanate, tested at up to 2500 ug/plate, was not mutagenic to Salmonella typhimurium TA1535, TA1538, TA98 or TA100 in the presence of a metabolic system from the liver of Aroclor-induced rats.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 307 (1986)]**PEER REVIEWED**

Disposal Methods :

Concentrated wastes from distillation equipment are preferably burnt in special waste incinerators. This also holds for complex and concentrated wastes, which cannot be regenerated by distillation. Because of the high reactivity of TDI /**toluene** diisocyanate/ waste waters contain only reaction products from the reaction with water. These can be biodegraded by treatment with activated sludge. Recommendable methods: Incineration, alkaline hydrolysis, discharge to sewer. Not recommendable: Landfill. Peer-review: Avoid contact or inhalation, add TDI to excess dilute alkali, and discharge to sewer. TDI can react explosively with moisture. (Peer-review conclusions of an IRPTC expert consultation (May 1985))
[United Nations. Treatment and Disposal Methods for Waste Chemicals (IRPTC File). Data Profile Series No. 5. Geneva, Switzerland: United Nations Environmental Programme, Dec. 1985. 101]**PEER REVIEWED**

Human Toxicity Excerpts :

Sera of 6 workers with conclusive evidence for IgE-mediated sensitization to isocyanates were used for evaluation of immunologic cross-reactivities among 8 different isocyanate-protein conjugates. In all cases radioallergosorbent test and/or skin-test investigations revealed the presence of IgE antibodies reacting specifically with human serum albumin conjugated with those isocyanates to which workers were exposed as well as with other isocyanates with which they were not in contact. By the radioallergosorbent test inhibition technique, moderate to strong mutual cross-reactivities between all tested isocyanate-human serum albumin conjugates, even between aromatics and aliphatics, were demonstrated in tests with 5 sera. One serum contained IgE antibodies that were almost completely specific to **toluene** diisocyanate-human serum albumin with this serum only weak cross-reactivities with other isocyanate conjugates were demonstrated. /Isocyanates/
[Baur X; J Allergy Clin Immunol 71 (2): 197-205 (1983)]**PEER REVIEWED**

Human Toxicity Excerpts :

A 47 yr old nonsmoking spray painter had an adenocarcinoma of the lung. He had been exposed to **toluene** diisocyanate and 4,4'-methylenediphenyl diisocyanate for 15 yr and had a 10 yr history of lung disease thought to be caused by exposure to isocyanates. /Isocyanates/
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 311 (1986)]**PEER REVIEWED**

Non-Human Toxicity Excerpts :

A number of industrial chemicals induce hypersensitivity responses in employees. 2,4-**Toluene** diisocynate (TDI) can cause pulmonary sensitization and allergic skin reactions. Since many commercial materials contain TDI, a study was designed to determine the concentration dependent elicitation of dermal sensitization in guinea pigs treated with TDI. Young adult guinea pigs received 2 open, epicutaneous induction applications (25 ul) of 8, 20 or 40% TDI in n-butyl ether on 2 separate areas. Five days later, animals were challenged with 0.0, 0.025, 0.05, 0.1, 0.2 and 0.4% TDI (25 ul per concentration site). All challange applications except the 0.0% solution elicited a positive response in 75-100% of the animals, and the severity of the skin reactions was dependent on the concentrations of the challenge and induction application. In another study using lower doses, animals received a total induction application (25 ul per each of 2 sites) of either 4 or 8% TDI and were challenged with 0.0, 0.006, 0.012, 0.025, 0.05 and 0.1% of TDI (25 ul per site). TDI did not elicit a sensitization response at challenge concentrations up to 0.012% (total application of 3 ug) when a 4% induction application was used, while a challenge concentration of 0.025% (total application of 6.25 ug) elicited a sensitization response in 63% of the animals. At the 8% induction application (total application of 4000 ug), all challenges, except the 0.0% indicated sensitization, and the intensities of the skin reactions were correlated with the challenge concentrations and the induction application. TDI produced sensitization at dilute induction concentrations and the severity of the dermal response was correlated with the concentration used at induction and challenge. No observed effect levels were determined below which the challenge concentration did not elicit a dermal hypersensitivity reaction. When 4% TDI was applied at induction, no observed effect was seen with a dermal challenge application of 3 ug whereas an effect was seen with 6.25 ug (in 35 ul) when n-butyl ether was the solvent.
[Koschier FJ et al; Toxicol Appl Pharmacol 67 (3): 401-7 (1983)]**PEER REVIEWED**

Medical Surveillance :

COMPLETE BIOLOGIC MONITORING, INCL PULMONARY FUNCTION & IMMUNOLOGIC STUDIES, HAS BEEN PERFORMED CONCURRENTLY WITH COMPREHENSIVE ENVIRONMENTAL MONITORING PROGRAM IN A PLANT MANUFACTURING **TOLUENE** 2,4-DIISOCYANATE.
[WEILL H ET AL; ENVIRON HEALTH PERSPECT 11: 101-8 (1975)]**PEER REVIEWED**

Special Reports :

NIOSH Current Intelligence Bulletin 53: **Toluene** diisocyanate and Toluenediamine; MMWR 40 (11): 189 (1991).

Analytic Laboratory Methods :

NIOSH Method: 141. Analyte: 2,4-**Toluene** diisocyanate. Matrix: Air. Procedure: Colorimetry. Method Evaluation: Method was validated over the range of 1.0 to 20.0 ug/cu m using a 20 liter sample. Precision (CVt): Unknown. Interferences: Any free aromatic amine may give a coupling color and thus may be a positive interference.
[U.S. Department of Health, Education Welfare, Public Health Service. Center for Disease Control, National Institute for Occupational Safety Health. NIOSH Manual ofAnalytical Methods. 2nd ed. Volumes 1-7. Washington, DC: U.S. Government Printing Office, 1977-present.,p. 141-1]**PEER REVIEWED**

Special Reports :

Dharmarajan V et al; Am Ind Hyg Assoc J 47 (7): 393-8 (1986). Two brands of air-purifying organic vapor cartridges ... and a disposable respirator ... were evaluated for protection against **toluene** diisocyanate vapors. ...

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Non-Human Toxicity Excerpts:

The effect of exposure to **toluene** diisocyanate vapor on pulmonary performance was studied in guinea pigs. Female English smooth haired guinea pigs were exposed to 1.4 ppm **toluene** diisocyanate vapor or air for 3 hours per day for 4 days, or to 0.02 ppm **toluene** diisocyanate for 6 hours per day for 70 days. Pulmonary performance was evaluated by the ventilatory response of the animals to 10% carbon dioxide. Serum antibodies to **toluene** diisocyanate were measured on days 22 and 50 and **toluene** diisocyanate pulmonary hypersensitivity was measured on days 37 and 38. Lung tissue histopathology was evaluated in all animals on day 50 following **toluene** diisocyanate exposure. Pulmonary response to 10% carbon dioxide diminished by 30 to 50% following **toluene** diisocyanate exposures at 1.4 ppm up to day 14. The ventilatory response showed recovery during the next 5 weeks. In contrast, animals exposed to 0.02 ppm **toluene** diisocyanate daily for 70 days showed no change in ventilatory response, nor did control animals that were not exposed to **toluene** diisocyanate. Antibodies were detected on day 22 and pulmonary hyprsensitivity to **toluene** diisocyanate was found in all animals exposed to 1.4 ppm **toluene** diisocyanate. No antibodies to **toluene** diisocyanate nor pulmonary hypersensitivity were detected in animals exposed to 0.02 ppm **toluene** diisocyanate or in control animals. Lung tissue on day 50 in the 1.4 ppm **toluene** diisocyanate exposed animals showed multifocal subchronic interstitial inflammation, localized pleural thickening, and peripheral lymphoid hyperplasia. No apparent abnormalities were observed in lung tissue of the 0.02 ppm exposed group. Exposure to 1.4 or 0.02 ppm **toluene** diisocyanate resulted in measurable and no apparent pulmonary toxicity in guinea pigs, respectively. The 10 percent carbon dioxide challenge provide several advantages for measuring pulmonary function. [Wang KL et al; J Toxicol Environ Health 15 (1): 137-48 (1985)]**PEER REVIEWED**

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Non-Human Toxicity Excerpts:

Exposing guinea pigs to **toluene** diisocyanate causes an acute increase in airway responsiveness to inhaled acetylcholine. The mechanism of this increase in airway responsiveness is unknown. Capsaicin-sensitive afferent nerves and the tachykinins they release upon activation are important in controlling bronchomotor tone in guinea pigs. To determine whether tachykinins are important in **toluene** diisocyanate induced airway hyperresponsiveness, the effects of tachykinin depletion were studied using capsaicin, and competitive tachykinin antagonism, using (D-Argl, D-Pro2, D-Trp7.9, Leull) substance P, on **toluene** diisocyanate induced airway hyperresponsiveness. In 9 of 9 untreated animals, **toluene** diisocyanate exposure caused a large and significant increase in airway responsiveness to acetylcholine. The mean concentration of acetylcholine required to decrease specific airway conductance by 50% below baseline (the PD50) was 1.51% before **toluene** diisocyanate exposure and 0.17% after **toluene** diisocyanate exposure ($p < 0.0005$). Capsaicin treatment had no effect on the PD50 but prevented the **toluene** diisocyanate induced increase in airway responsiveness in 10 of 12 animals. (The PD50 was 1.03% before **toluene** diisocyanate and 1.27% after **toluene** diisocyanate exposure.) Treatment with the tachykinin antagonist (D-Argl, D-Pro2, D-Trp7.9, Leull) substance P also abolished the **toluene** diisocyanate induced increase in airway responsiveness in all 5 animals treated. Although **toluene** diisocyanate exposure also caused airway edema, the effect of capsaicin treatment on **toluene** diisocyanate induced hyperresponsiveness did not result from prevention of airway edema. **Toluene** diisocyanate exposure caused a marked increase in tracheal extravasation of intravenously administered Evans blue dye that was not prevented by capsaicin treatment.
[Thompson JE et al; Am Rev Respir Dis 136 (1): 43-9 (1987)]**PEER REVIEWED**

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Metabolism/Metabolites:

It has been previously shown that tachykinin depletion or antagonism prevented the increase in airway responsiveness to inhaled acetylcholine caused by exposure to **toluene** diisocyanate in awake guinea pigs. To insure that the effects of tachykinins were not limited to the extrathoracic airways and were not dependent on effects of **toluene** diisocyanate on baseline airway caliber, airway responsiveness to acetylcholine inhaled through tracheostomy in anesthetized and ventilated guinea pigs that were exposed to **toluene** diisocyanate or air after treatment with the tachykinin antagonist spantide, the tachykinin metabolism inhibitor phosphoramidon, or the vehicles for each drug were determined. When these drugs were administered before and during **toluene** diisocyanate exposure, spantide significantly inhibited the **toluene** diisocyanate induced increase in acetylcholine responsiveness and phosphoramidon significantly potentiated this effect, whereas neither drug altered acetylcholine responsiveness in air exposed animals. To determine whether tachykinins were exerting their effect primarily during **toluene** diisocyanate exposure or during the subsequent acetylcholine challenge, the effect of each drug on acetylcholine responsiveness was also examined when the drugs were given after **toluene** diisocyanate exposure. At that time, spantide did not inhibit **toluene** diisocyanate induced acetylcholine hyperresponsiveness and phosphoramidon did not potentiate it. Neither drug nor **toluene** diisocyanate increased pulmonary resistance measured through a tracheostomy in these anesthetized and ventilated animals. These results suggest that the **toluene** diisocyanate induced increase in acetylcholine responsiveness is mediated by release of tachykinins into the intrathoracic airways during exposure to **toluene** diisocyanate.
[Sheppard D, Scypinski L; Am Rev Respir Dis 138 (3): 547-51 (1988)]**PEER REVIEWED**

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Mechanism of Action:

The effects of **toluene** diisocyanate on T-cell subpopulations and circulating lymphocytes in ten persons (five males)): 19 to 50 yr old, with **toluene** diisocyanate induced occupational asthma were examined. Five subjects revealed early and late asthmatic reactions to **toluene** diisocyanate (dual responders) and five revealed late asthmatic reactions (late responders). Subjects underwent inhalation challenge with 0.005 to 0.015 ppm **toluene** diisocyanate or filtered air for 10 to 30 min on two occasions. One second forced expiratory volumes were measured before and at periodic intervals between 30 min and 24 hr after challenge. Venous blood samples were drawn 30 min and 8, 24, 48, and 72 hr after **toluene** diisocyanate. Total and differential leukocyte counts and T-cell subpopulations were determined. The five dual responders demonstrated forced expiratory volume in 1 sec decreased indicative of early and late asthmatic reactions and the five late responders demonstrated forced expiratory volume in 1 second decr indicative of a late asthmatic reaction. **Toluene** diisocyanate challenge did not affect the number of circulating erythrocytes and leukocytes. The percentage of eosinophils was significantly increased 24 hr after challenge and sustained for up to 48 hr. The percentages of neutrophils, lymphocytes, and monocytes were not altered by **toluene** diisocyanate. Among the T-lymphocyte subpopulation, the proportion of CD8(+) lymphocytes was significantly increased 8 hr after **toluene** diisocyanate challenge. The increase was more pronounced in the lat responders. An additional increase in CD8(+) lymphocytes occurred 48 hr post exposure in seven subjects but was unrelated to responder type. The number of CD4(+) cells did not change. This resulted in a decrease in the CD4(+)/CD8(+) ratio 8 and 48 hr after **toluene** diisocyanate challenge. It was concluded that **toluene** diisocyanate induced late asthmatic reactions are associated with an increase in the number of suppressor/cytotoxic lymphocytes and eosinophils in peripheral blood.

[Finotto S et al; Br J Ind Med 48 (2):116-21 (1991)]**PEER REVIEWED**

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Non-Human Toxicity Excerpts:

Toluene diisocyanate is a causative agent in occupational asthma. Through an oral catheter **toluene** diisocyanate, 0.03 ul, dissolved in 0.02 ml olive oil, was superfused on the tracheobronchial mucosa of anaesthetized guinea pigs. **Toluene** diisocyanate induced plasma exudation into both airway tissue and lumen (peak effect: 5 hr; duration approximately 17 hr). Light microscopy examinations demonstrated that the epithelium was not disrupted by this process (and that microvessels are abundant just beneath the epithelium). At days 6 and 21 after exposure to **toluene** diisocyanate PAS-positive cells were increased, but no other histological alterations were found. Also, the occurrence of peptide containing nerve fibres was not altered by **toluene** diisocyanate. After **toluene** diisocyanate exposure the airway smooth muscle tone was elevated as examined in vitro at base-line and at conc response to carbachol. The largest incr in tone were recorded 21 days after exposure to **toluene** diisocyanate. The abnormally large tone was not associated with an increased thickness of the smooth muscle layer nor was it associated with reduced effects of either beta 2-agonist (terbutaline) or xanthine (theophylline) relaxants. It is concluded that **toluene** diisocyanate induced plasma exudation into guinea pig airways for 17 hr without disrupting the epithelial lining and without causing major changes in the airway peptidergic innervation. Both the airway tone, and the number of mucous cells, are increased for at least 3 wk after exposure to **toluene** diisocyanate.

[Persson CG et al; Clin Exp Allergy 21 (6): 715-24 (1991)]**PEER REVIEWED**

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Mechanism of Action:

Serum neutrophil chemotactic activity, which is associated with mast cell or basophil activation, was quantitated to determine if mast cell or basophil mediators are released during bronchoprovocation-inhalation challenge with subirritant levels of **toluene** diisocyanate. Four subjects with suspected **toluene** diisocyanate induced asthma and four mite-sensitive subjects with asthma who served as a comparison group were studied. neutrophil chemotactic activity was measured in a multiwell, microchemotaxis chamber. Blood samples were collected, and forced expiratory volume in 1 second measurements were performed before challenge and at regular intervals during the subsequent 24 hr. Three of four workers clinically sensitive to **toluene** diisocyanate reacted to a subirritant **toluene** diisocyanate exposure. There was no increase in neutrophil chemotactic activity during placebo challenges. neutrophil chemotactic activity increased in the three **toluene** diisocyanate sensitive workers during early and late asthmatic reactions in quantities proportional to the forced expiratory volume in 1 second decline. No increase in neutrophil chemotactic activity was found during **toluene** diisocyanate exposures in the **toluene** diisocyanate negative worker. Gel filtration analysis demonstrated the main neutrophil chemotactic activity fraction eluted with macromolecules of an estimated molecular weight greater than 440,000 daltons. This characteristic is compatible with neutrophil chemotactic factor of basophil or mast cell origin. The kinetics of neutrophil chemotactic activity release were similar in mite- and **toluene** diisocyanate induced asthmatic reactions. A high correlation ($r = 0.97$; $p = 0.0006$) was obtained between the percent decrease in forced expiratory volume in 1 second during early asthmatic reactions and percent increase in neutrophil chemotactic activity. These observations support the hypothesis that activation of mast cells or basophils is associated with **toluene** diisocyanate induced early and late asthmatic reaction.

[Sastre J et al; J Allergy Clin Immunol 85 (3): 567-72 (1990)]**PEER REVIEWED**

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Human Toxicity Excerpts:

The mechanism by which late asthmatic reactions are induced by **toluene** diisocyanate, a low molecular weight chemical that causes occupational asthma in exposed subjects, is unknown. An investigation was conducted to determine whether early and late asthmatic reactions induced by **toluene** diisocyanate are associated with changes in airway responsiveness to methacholine and airway inflammation as determined by bronchoalveolar lavage. Forced expiratory volume in 1 second was measured before and at regular intervals after exposure to **toluene** diisocyanate and dose-response curves to methacholine and bronchoalveolar lavage at 8 hr after **toluene** diisocyanate /were performed/ in a group of 6 subjects with late asthmatic reactions and in 6 subjects with only early asthmatic reactions. The same procedure was followed 2 hr after **toluene** diisocyanate in a group of 6 subjects with previously documented late asthmatic reactions and in a group of 6 subjects without any previously documented asthmatic reaction after **toluene** diisocyanate. In subjects with late asthmatic reactions, neutrophils were increased at both 2 hr and 8 hr and eosinophils and airway responsiveness were increased only at 8 hr. By contrast, neutrophils, eosinophils and airway responsiveness were not increased at 8 hr after **toluene** diisocyanate in subjectswith an early asthmatic reaction or at 2 hr after **toluene** diisocyanate in normal control subjects. These results suggest that late asthmatic reactions to **toluene** diisocyanate, and the associated increase in airway responsiveness may be caused by airway inflammation.
[Fabbri LM et al; Am Rev Respir Dis 136 (1): 36-42 (1987)]**PEER REVIEWED**

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Human Toxicity Excerpts:

Six workers with occupational asthma due to **toluene** diisocyanate were studied. For each worker a detailed clinical and occupational history was taken, and lung function measurement and skin intradermal tests for common allergens were carried out. Methacholine inhalation challenge was performed before **toluene** diisocyanate inhalation, and 8 hr after **toluene** diisocyanate inhalation. Methacholine challenge was within normal limits when performed before **toluene** diisocyanate inhalation, but went into the asthmatic range after **toluene** diisocyanate inhalation. These cases provid evidence that asthma can be induced by **toluene** diisocyanate in the absence of airway hyperresponsiveness. They further demonstrate that an isolated negative methacholine inhalation test cannot be used to exclude sensitization to **toluene** diisocyanate. Screening and follow-up studies on workers exposed on **toluene** diisocyanate require serial measurements of airway responsiveness and of variable air-flow obstruction.
[Mapp CE et al; Eur J Respir Dis 68 (2): 89-95 (1986)]**PEER REVIEWED**

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Human Toxicity Excerpts:

Forty-three workers exposed to low levels of **toluene** diisocyanate during the process of producing polyurethane forms were examined immunologically for immunoglobulin-G, A, M, and E and serum enzyme activities such as serum angiotensin converting enzyme, serum lysozyme and glycylproline dipeptidyl aminopeptidase. Air concn of **toluene** diisocyanate was annually measured in various places of work during the past five years from 1979 to 1983. The results obtained in the present study were as follows. The air concn of **toluene** diisocyanate at all places of work was below the permissible concn level of 0.02 ppm throughout the study period. Subjective symptoms and abnormal findings on chest X-ray considered directly related to **toluene** diisocyanate exposure were no observed. No remarkable abnormal findings in blood cell counts and in serum biochemical studies could be seen in any of the workers. The serum immunoglobulin-G levels in workers directly exposed to **toluene** diisocyanate were significantly higher ($p < 0.05$) than those in workers indirectly exposed to **toluene** diisocyanate and in non-exposed workers. In the study of serum enzymatic activity, serum lysozyme activity in workers exposed directly to **toluene** diisocyanate was significantly higher ($p < 0.01$) than those in workers indirectly exposed to **toluene** diisocyanate and in non-exposed workers.
[Taniwaki H et al; Sangyo Igaku 29 (2): 130-5 (1987)]**PEER REVIEWED**

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Metabolism/Metabolites:

Five men were exposed to **toluene** diisocyanate atmospheres for 7.5 hr. The **toluene** diisocyanate atmospheres were generated by a gas-phase permeation method, and the exposures were performed in an 8 cu m stainless steel test chamber. The mean air concn of **toluene** diisocyanate was ca 40 ug/cu m, which corresponds to the TLV of Sweden. The inhaled doses of 2,4- and 2,6-**toluene** diisocyanate were ca 120 ug. **Toluene** diisocyanate in the test chamber air was determined by an HPLC method using the 9-(N-methylaminomethyl)-anthracene reagent and by a continuous monitoring filter-tape instrument. After hydrolysis of plasma and urine, the related amines, 2,4- and 2,6-toluenediamine 2,4-, and 2,6-TDA), were determined as pentafluoropropionic anhydride derivatives by capillary gas-chromatography using selected ion monitoring in the electron-impact mode. The urinary elimination of the toluenediamines showed a possible biphasic pattern, with rapid first phases for 2,4-toluenediamine (mean half-life for the concn in urine, 1.9 hr) and for 2,6-toluenediamine (mean half-life for the concn in urine, 1.6 hr). The cumulative amount of 2,4-toluenediamine excreted in urine within 28 hr ranged from 8% to 14% of the estimated dose of 2,4-**toluene** diisocyanate, and the cumulative amount of 2,6-toluenediamine in urine ranged from 14% to 18% of the 2,6-**toluene** diisocyanate dose. The average urinary level of 2,4-toluenediamine was 5 ug/l in the 6 to 8 hr sample (range 2.8-9.6 ug/l), and the corresponding value fo 2,6-toluenediamine was 8.6 ug/l (range, 5.6-16.6 ug/l). Biological monitoring of exposure to 2,4- and 2,6-**toluene** diisocyanate by analysis of 2,4- and 2,6-toluenediamine in urine is feasible.
[Skarping G et al; Int Arch Occup Environ Health 63 (2): 83-8 (1991)]**PEER REVIEWED**

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Human Toxicity Excerpts:

To determine whether late asthmatic reactions and the associated increase in airway induced by **toluene** diisocyanate are linked to airway inflammation, inhibition by prednisone was investigated. Ten "sensitized" subjects were studied in 2 sets of experiments. In the first set, each subject was given no treatment and was studied before and for 8 hr after exposure to **toluene** diisocyanate. In the second set, 2 to 4 wk later, each subject was studied before treatment and then during treatment with prednisone (50 mg once a day for 3 days, orally), both before and after exposure to **toluene** diisocyanate. To assess late asthmatic reactions to **toluene** diisocyanate FEV1 /was measured/ immediately before and after exposure, then hourly for 8 hr. To assess changes in airway responsiveness, a /measurement was made of/ the provocation dose (mg) of methacholine causing a 20% decrease in FEV1 (PD20FEV1) before and 8 hr after exposure to **toluene** diisocyanate. When the subjects received no prednisione treatment, **toluene** diisocyanate caused late asthmatic reactions and increased airway responsiveness. By contrast, when the subjects received prednisone, **toluene** diisocyanate caused no late asthmatic reaction or increased airway responsiveness. Prednisone did not change baseline airway caliber or airway responsiveness. These results suggest that late asthmatic reactions and the associated increase in airway responsiveness induced by **toluene** diisocyanate in "sensitized" subjects may depend on the development of a steroid-responsive acute inflammatory reaction within the airways.
[Fabbri LM; Am Rev Respir Dis 132 (5): 1010-4 (1985)]**PEER REVIEWED**

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Human Toxicity Excerpts:

A worker developed **toluene** diisocyanate induced asthma in 1974. On reassessment, 11 yr after leaving the chemical plant where **toluene** diisocyanate was produced, he had no respiratory symptoms and normal bronchial reactivity in response to methacholine, and showed no reaction when challenged with a subirritant concn of **toluene** diisocyanate. He developed asthma within five months of returning to the workplace. Repeat challenge testing showed bronchial hyperreactivity to methacholine and to the specific sensitising agent, **toluene** diisocyanate. This clinical pattern could be due to underlying **toluene** diisocyanate sensitivity with resolution and reappearance of hyperresponsiveness to methacholine and **toluene** diisocyanate reactivity associated with workplace **toluene** diisocyanate exposure. Alternatively, this worker may have developed sensitisation to **toluene** diisocyanate anew.
[Banks DE, Rando RJ; Thorax 43 (8): 1988 660-2]**PEER REVIEWED**

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Mechanism of Action:

Leukotriene B4 release from the lungs of sensitized subjects during asthmatic reactions induced by **toluene** diisocyanate was investigated. Three groups of **toluene** diisocyanate sensitized subjects were examined, one after no exposure to **toluene** diisocyanate, the second 8 hr after an exposure to **toluene** diisocyanate that caused an early asthmatic reaction, and the third 8 hr after an exposure to **toluene** diisocyanate that caused a late asthmatic reaction. Bronchoalveolar lavage fluid was analysed by reverse-phase HPLC and by specific radioimmunoassay. The mean concn of leukotriene B4 was higher (0.31 + or - 0.09 (standard error) ng/ml, range 0.15-0.51) in bronchoalveolar lavage fluid of sensitized subjects who developed a late asthmatic reaction than in bronchoalveolar lavage fluid of subjects who developed an early asthmatic reaction (0.05 + or - 0.04 ng/ml, range 0-0.224), and no leukotriene B4 was detectable in the control subjects. Bronchoalveolar lavage was also performed 8 hr after **toluene** diisocyanate exposure on four **toluene** diisocyanate sensitized late-dual reactors who were on steroid treatment. In this group of subjects no leukotriene B4 was detectable. These results suggest that leukotriene B4 may be involved in late asthmatic reactions induced by **toluene** diisocyanate.
[Zocca E et al; J Appl Physiol 68 (4): 576-80 (1990)]**PEER REVIEWED**

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Interactions:

The effects of methacholine inhalation on airway responsiveness in **toluene** diisocyanate induced asthma were studied in six workers with a history of sensitivity to **toluene** diisocyanate. Symptoms among subjects included shortness of breath, wheezing, cough, and chest tightness at work, during the evening, or at night. A detailed cllnical and occupational history was taken for each subject, and lung function measurement and skin intradermal tests for common allergens were conducted. Airway responsiveness to methacholine was assessed before subjects were exposed for 30 minutes to 0.02 part per million **toluene** diisocyanate in an exposure chamber. Eight hours after **toluene** diisocyanate inhalation, airway responsiveness to methacholine was again determined. Forced expiratory volume was the measure of airway responsiveness. Although methacholine challenge was within normal limits when performed before **toluene** diisocyanate inhalation, the challenge went into the asthmatic range after **toluene** diisocyanate inhalation. Airway responsiveness increased significantly 8 hours after **toluene** diisocyanate challenge in the subjects and was accompanied by a decrease in forced expiratory volume. The late asthmatic reaction began between 3 and 5 hours asthma can be induced by **toluene** diisocyanate in the absence of airway responsiveness.
[Mapp CE et al; Eur J Respir Dis 68: 89-95 (1986)]**PEER REVIEWED**

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Protective Equipment & Clothing:

Three commercial air-purifying respirators for protection against **toluene** diisocyanate vapors were evaluated. The Willson R-21 and Survivair, organic vapor cartridges, and the disposable, valveless 3M-8711 were the three respirators evaluated. Each respirator/cartridge was tested three times at 0.2 ppm **toluene** diisocyanate concn for 40 hr and once for 20 hr or more at concn greater than 1.5 ppm **toluene** diisocyanate. All cartridges/respirators had the capacity to provide the required protection against **toluene** diisocyanate vapors. Additional considerations in the respirator selection process included the training and experience of the respirator user, the enforcement of the respirator program, fit of the respirator, knowledge of **toluene** diisocyanate concn onsite, presence of other solvents or chemicals in the air which may adversely affect the capacity of the respirato for **toluene** diisocyanate, and the high odor threshold of **toluene** diisocyanate that makes it impossible for the user to receive advance warning of a leak.

[Dharmarajan V et al; Am Ind Hyg Assoc 47 (7): 393-8 (1986)]**PEER REVIEWED**

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Analytic Laboratory Methods:

A solvent free sampling method for airborne **toluene** diisocyanate was described. Air samples were collected on quartz fiber filters impregnated with 1-(2-methoxyphenyl)piperazine. **Toluene** diisocyanate in the samples reacted with 1-(2-methoxyphenyl)piperazine to form urea derivatives which after dissolution in methanol were analyzed by reversed or normal phase HPLC. When reversed phase HPLC was used, a C18 bonded phase column was utilized. A cyano amino bonded phase column was used with normal phase HPLC. An ultraviolet detector set at a wavelength 250 nanometers was also used. Detection limits for a 15 liter air sample based on a 5 mm peak height were 0.02 to 0.04 mg/cu m, corresponding to 0.5 to 1 nanograms of **toluene** diisocyanate injected. The method was used to sample laboratory generated **toluene** diisocyanate containing atmospheres over the relative humidity range 11 to 75% and temperature range 20 to 50 deg C. In the study of the effects of humidity, samples were also collected with gas bubblers and silica gel tubes for comparison purposes. **toluene** diisocyanate concn in the collected samples increased linearly with incr temperature. When the samples were collected on the 1-(2-methoxyphenyl)piperazine coated fibers the collected **toluene** diisocyanate concn were not affected by changes in relative humidity. Collection efficiency of the bubblers and silica gel tubes decr for humidities in excess of 45%. It was concluded that the 1-(2-methoxyphenyl)piperazine impregnated quartz fiber filter method for **toluene** diisocyanate sampling is convenient and efficient, and that collection efficiency does not appear to be affected by humidity.
[Robert A, Simon P; Chromatographia 23 (7):507-11 (1987)]**PEER REVIEWED**

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Human Toxicity Excerpts:

An outbreak of occupational asthma due to **toluene** diisocyanate among industrial workers was described. Four employees at a velcro/like tape manufacturing factory in Taipei, Taiwan were seen in an outpatient clinic complaining of cough, shortness of breath, and wheezing. The symptoms became worse at night and improved after long holidays. The patients' job involved applying an adhesive to the tape. Thirty eight of 45 employees were interviewed by questionnaire and given pulmonary function tests. The pulmonary function tests were given during a workday, after a 10 day holiday, and 5 mo after control measures such as process isolation, improved ventilation, and substitution for **toluene** diisocyanate were instituted. Industrial hygiene sampling for **toluene** diisocyanate was conducted. Fourteen workers had symptoms of asthma or asthmatic bronchitis. The highest attack rate occurred in workers employed in the tape processing area where the adhesive was applied. Workers in the tape processing area also showed the greatest decr in 1 second forced expiratory volume and forced vital capacity over the workday. Mean **toluene** diisocyanate concn ranged from 0.012 to 0.047 ppm, the highest occurring in the tape processing area and the lowest in the weaving area. The prevalence of asthmatic symptoms was significantly correlated with **toluene** diisocyanate concn. The forced expiratory volume in 1 second and forced vital capacity values were significantly improved after the 10 day holiday and 5 mo after the control methods were instituted. No asthmatic symptoms were reported after 5 mo. It was concluded that **toluene** diisocyanate was responsible for the outbreak and improving the work environment was effective in reducing exposure to **toluene** diisocyanate.
[Wang JD et al; Am J Ind Med 14 (1): 73-8 (1988)]**PEER REVIEWED**

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Human Toxicity Excerpts:

The effect of cessation of exposure to **toluene** diisocyanate was studied in six patients with **toluene** diisocyanate induced asthma, proved by a positive inhalation challenge with **toluene** diisocyanate. Bronchial challenges with **toluene** diisocyanate and methacholine were performed, and lobar bronchial biopsies were taken at diagnosis and 6 mo later, after cessation of exposure. Biopsies from four nonasthmatic control subjects were also examined. At diagnosis, asthmatic subjects had thickened reticular basement membrane ($p < 0.05$) and increased numbers of mononuclear cells ($p < 0.05$) and eosinophils ($p < 0.05$) in the lamina propria when compared with control subjects. Electron microscopy showed degranulation of eosinophils and mast cells in asthmatics. Six months after cessation of exposure, the thickness of reticular basement membrane was significantly reduced compared with that at diagnosis ($p < 0.05$), and it decr to values similar to those of control biopsies. Inflammatory cell numbers in bronchial mucosa of asthmatic subjects did not change significantly 6 mo after removal from exposure, and degranulation of eosinophils and mast cells was still present. At the end of the study, airwa hyperresponsiveness to methacholine and/or sensitivity to **toluene** diisocyanate persisted in most of the asthmatic patients despite the cessation of exposure and the disappearance of asthmatic symptoms. In conclusion, in patients with occupational asthma induced by **toluene** diisocyanate, the avoidance of exposure to the sensitizing agent for 6 mo is able to reverse the reticular basement membrane thickening in the bronchial mucosa, but th inflammatory cell infiltrate, the specific sensitivity to **toluene** diisocyanate, and the nonspecific airway hyperreactivity may persist.
[Saetta M et al; Am Rev Respir Dis 145 (1): 169-74 (1992)]**PEER REVIEWED**

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Human Toxicity Excerpts:

Among the painters handling polyurethane varnish in two furniture manufacturing factories with high **toluene** diisocyanate exposure (0.79 mg/cu m and 0.31 mg/cu m), 26.3% and 15% subjects, respectively displayed asthmatic symptoms, lung function loss, and an increment in mast cell degranulation percentage specific to **toluene** diisocyanate. Some cases of **toluene** diisocyanate linked contact dermatitis were also found among them, being elucidated by positive patch testing to **toluene** diisocyanate. However, the previous abnormalities could not be verified among the painters from another factory with **toluene** diisocyanate concn below the TLV of it (0.11 mg/cu m). It was concluded that both pulmonary hypersensitivity and contact sensitization to **toluene** diisocyanate had occurred in some of the painters included in this study, and that the immunologic effects of **toluene** diisocyanate was concn dependent.

[Huang J et al; Arch Environ Contam Toxicol 21 (4): 607-11 (1991)]**PEER REVIEWED**

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Human Toxicity Excerpts:

Pulmonary function tests were done and compared to current and past potential exposure levels of **toluene** diisocyanate for 57 **toluene** diisocyanate manufacturing workers and 89 workers not exposed to **toluene** diisocyanate or other known respiratory hazards. The average **toluene** diisocyanate plant experience was 4.1 yr (standard deviation = 2.8). Routine industrial hygiene measurements have shown **toluene** diisocyanate exposure below a time-weighted average of 0.005 ppm and a short-term exposure level of 0.02 ppm. A certified industrial hygienist ranked department and job classification by level of potential exposure to **toluene** diisocyanate (none, low, moderate, and high). A questionnaire was administered to determine the prevalence of respiratory symptoms and smoking habits. Using backward regression analysis, cumulative pack-years of cigarette smoking and prevalence of lower respiratory symptoms were statistically significant predictors of a standardized forced expiratory volume at 1 second; however, **toluene** diisocyanate exposure, whether classified as current, highest career level, cumulative, or cumulative highest-to-date, was not associated with a decline in forced expiratory volume. [Olsen GW et al; J Occup Med 31 (8): 664-7 (1989)]**PEER REVIEWED**

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Mechanism of Action:

Isocyanates are an important cause of occupational asthma. The mechanism of isocyanate induced asthma is still unknown. To determine whether **toluene** diisocyanate stimulates the 'efferent' function of peripheral endings of capsaicin-sensitive sensory nerves, we investigated the effect of **toluene** diisocyanate in the rat isolated urinary bladder, a preparation in which the action of capsaicin has been well characterized. **Toluene** diisocyanate (0.03 mM) produced a concn dependent contraction of the bladder strips. It maximal effect was about 50 % of the response to capsaicin (1 uM). Previous exposure of the strips to capsaicin followed by washing out produced complete unresponsiveness, both to the first exposure to **toluene** diisocyanate and to a second exposure of capsaicin. Further, the response to both **toluene** diisocyanate and capsaicin was completely prevented by extrinsic bladder denervation, achieved by bilateral removal of pelvic ganglia (72 hr before). Repeated exposure of the rat bladder to **toluene** diisocyanate reduced the capsaicin-evoked release of calcitonin gene-related peptide like immunoreactivity (CGRP-LI), taken as biochemical marker of activation of these sensory nerves. These experiments provide the first evidence that **toluene** diisocyanate activates directly or indirectly the efferent function of capsaicin-sensitive primary sensory nerves.
[Mapp CE et al; Eur J Pharmacol 180 (1): 113-8 (1990)]**PEER REVIEWED**

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Non-Human Toxicity Excerpts:

The **toluene** diisocyanate induced delayed type hypersensitivity reaction in the ear of male mice was investigated and compared with the picryl chloride induced one. The results obtained were as follows: 1) When 1% **toluene** diisocyanate solution (20 ul/ear) as a challenging concentration was used for 7 week old ICR mice, distinct ear swelling was observed in every group sensitized with various concentrations (1-5%, 100 ul/animal) of **toluene** diisocyanate solution, and the swelling rate was the same or higher than that of picryl chloride induced delayed type hypersensitivity. 2) Five, 7 and 13 week old ICR mice showed a similar high response in TDI induced delayed type hypersensitivity, whereas the reactivity of 16 week old ICR mice was significantly lower than that of the above mentioned younger mice. 3) In both **toluene** diisocyanate and picryl chloride induced delayed type hypersensitivity reaction, ICR and BALB/c mice showed a similar high response, whereas the reactivity of ddY mice was significantly lower. The effects of dexamethasone and indomethacin were investigated with the **toluene** diisocyanate induced delayed type hypersensitivity model. The delayed type hypersensitivity reaction was suppressed significantly by both drugs, but the suppressive effects of dexamethasone were higher than that of indomethacin. All the above results indicate that the **toluene** diisocyanate induced delayed type hypersensitivity model in mice taking dye leakage as an index may be useful for evaluation of drugs for disorders derived from delayed type hypersensitivity reactions.
[Tominaga M et al; Jpn J Pharmacol 39 (2): 163-71 (1985)]**PEER REVIEWED**

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Non-Human Toxicity Excerpts:

The changes in airway responsiveness to increasing doses of an acetylcholine aerosol in anesthetized and ventilated guinea pigs 2, 6, or 24 hr after exposure to air or 1 ppm **toluene** diisocyanate were examined. Pulmonary resistance after the animals inhaled a buffered saline aerosol was used as baseline and was similar for air and groups. The concentration of acetylcholine calculated to cause a 200% increase in pulmonary resistance was significantly lower for animals studied at 2 hr (0.68%) or at 6 hr (0.77%), but not at 24 hr (2.39%), after than for air animals (3.07%). The increase in airway responsiveness in the exposed animals was associated with histologic changes in the trachea and intrapulmonary airways. Exposure to 2 ppm caused a patchy loss of cilia, shedding of epithelial cells into the airway lumen, and an influx of inflammatory cells into the trachea and other airways. In the lamina propria of the trachea, the concentration of extravascular polymorphonuclear leukocytes was 13 to 26-fold greater in animals studied 2 or 6 hr after exposure to 2 ppm **toluene** diisocyanate or at 2 hr after 1 ppm **toluene** diisocyanate than in animals exposed to air. The concentration of polymorphonuclear leukocytes in the epithelium was significantly increased only in animals examined 2 hr after 2 ppm **toluene** diisocyanate. Exposure to **toluene** diisocyanate also caused an influx of eosinophils into the tracheal mucosa. This influx occurred later and was more persistent than the influx of polymorphonuclear leukocytes. These results indicate that a single exposure to **toluene** diisocyanate can cause an increase in airway responsiveness that is associated with epithelial injury and acute airwayinflammation.
[Gordon T et al; Am Rev Respir Dis 132 (5): 1106-12 (1985)]**PEER REVIEWED**

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Human Toxicity Excerpts:

A study of individuals with occupational asthma induced by **toluene** diisocyanate was conducted. This was a followup of 35 patients, 25 males, with a history of isocyanate sensitization. They had 3 to 41 years' occupational exposure to isocyanate compounds. The subjects had been diagnosed with isocyanate asthma on the basis of their response to bronchial challenge with **toluene** diisocyanate. They were examined an average of 11 mo after diagnosis. They underwent bronchial challenge with **toluene** diisocyanate and methacholine. Forced expiratory volumes in 1 second were measured. Symptoms reported by the subjects were recorded. Twenty seven subjects were still asthmatic at followup as shown by a positive reaction to **toluene** diisocyanate challenge. They showed a deterioration in their forced expiratory volumes in 1 second and response to methacholine similar to that seen at diagnosis. Seventy seven percent of these subjects continued to have recurring attacks of dyspnea, wheezing, and cough which required medication. Twenty two of the asthma subjects had been removed from exposure. Subjects who recovered (did not react to **toluene** diisocyanate at the followup examination) showed an improvement in their forced expiratory volumes in 1 second and a reduced response to methacholine. At the time of diagnosis they tended to have an immediate or dual asthmatic reaction and were younger than the other subjects. The asthmatic subjects had dual or late reactions at diagnosis. It was concluded that respiratory symptoms, isocyanate sensitization, and airway hyperresponsiveness may persist for some time after exposure to **toluene** diisocyanate has ended.
[Mapp CE et al; Am Rev Respir Dis 137 (6): 1326-9 (1988)]**PEER REVIEWED**

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Metabolism/Metabolites:

A technique for detectingurinary amine metabolites in rats exposed to **toluene** diisocyanate was evaluated. Skin tissue of rats was exposed to 40% **toluene**-2,4-diisocyanate solution in di-n-butyl-ether liquid. Rats were exposed daily for 3 hr on 4 consecutive days. Urine was collected in metabolic cages for 18 hr after the last exposure. Chromatographic techniques were used for nitrogen selective detection of nonderivatized amines. An autolinear temperature programmer was employed to analyze derivatized amine. The identity of the amine was confirmed by gas chromatography/mass spectrometry. A linear correlation was found between **toluene**-2,4-diamine added to urine and peak height. Peak height and recovery from the non hydrolyzed and from the hydrolyzed urine was about 85 and 70%, respectively. No free **toluene**-2,4-diamine or free **toluene**-2,4-diisocyanate was detected in the urine of rats exposed to **toluene**-2,4-diamine in hydrolyzed urine was 1.5 micrograms per milliliter. Gas chromatography/mass spectrometry confirmed the identity of the amine. /This/ highly sensitive technique tested is easy to apply and is effective for trace assays of amines.
[Rosenberg C; J Chromatography 323 (2): 429-33 (1985)]**PEER REVIEWED**

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Human Toxicity Excerpts:

Diisocyanate inhalation tests (maximal concn, 20 ppb; exposure time, 1-2 hr) were performed using **toluene** diisocyanate (TDI, n = 15) and diphenylmethane diisocyanate (MDI, n = 7) as well as methacholine challenges in 19 workers who had a clinical history of **toluene** diisocyanate/diphenylmethane diisocyanate induced asthma. Additionally volunteers were tested who had n previous contact with diisocyanates: 10 healthy individuals with a negative methacholine test and 14 patients with asthma and a positive methacholine test were exposed to **toluene** diisocyanate. In all, 1 of the normal volunteers and 3 of the patients with asthma unrelated to diisocyanates showed a positive airway reaction to **toluene** diisocyanate, and 13 of the 19 diisocyanate workers displayed a positive result in the **toluene** diisocyanate/diphenylmethane diisocyanate inhalation test; however, only 6 of these 13 individuals reacted to methacholine. Furthermore, 3 of the 6 patients with a negative **toluene** diisocyanate/diphenylmethane diisocyanate challenge test demonstrated a significant response to methacholine. It was concluded that bronchial hyperreactivity as evaluated by the methacholine challenge test is not closely related to isocyanate induced bronchoconstriction and, therefore, the metacholine challenge is only of limited diagnostic value in patients with suspected isocyanate induced asthma.

[Vogelmeier C et al; Int Arch Occup Environ Health 63 (1): 9-13 (1991)]**PEER REVIEWED**

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Mechanism of Action:

To determine whether early and/or late asthmatic responses induced by **toluene** diisocyanate are caused by a reflex mechanism involving stimulation of muscarinic receptors, we studied the effect of the muscarinic antagonist atropine on early and late airway response induced by **toluene** diisocyanate. A preliminary study was conducted in asthmatics to assess whether the selected dose of atropine provided adequate muscarinic blockade. On different days we measured the provocation dose (in mg) of carbachol causing a 15% decrease in forced expiratory volume in 1 second (PD15FEV1) without and with atropine premedication (0.008 or 0.012 mg/kg sc atropine 30 or 90 min before carbachol challenge test). 0.008 to 0.012 mg/kg sc atropine increased the PD15FEV1 carbachol by 6 to 10 fold, inducing a consistent and prolonged decrease in nonspecific bronchial hyperresponsiveness to cholinergic agent. 10 Subjects with a history of sensitization to **toluene** diisocyanate were then examined in 2 sets of experiments. In the first set of experiments, the subjects were studied before and after exposure to **toluene** diisocyanate (0.04 ppm; 30 min) after no treatment. In the second set of experiments, carried out 1 to 2 wk later, the same procedure was repeated after treatment with atropine (0.008 to 0.012 mg/kg atropine sulfate administered sc 30 min before **toluene** diisocyanate challenge, and then at 90 min intervals after **toluene** diisocyanate exposure); all patients showed symptoms of atropine effect (dryness of mouth, cycloplegia, increased heart rate).

[Paggiaro P et al; Am Rev Respir Dis 136 (5): 1237-41 (1987)]**PEER REVIEWED**

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Human Toxicity Excerpts:

An investigation of the persistence of isocyanate induced asthma in workers with negligible occupational exposure was carried out. Six asthmatic workers, proven to be **toluene** diisocyanate sensitive by inhalation challenge testing in a longitudinal study of respiratory health risks associated with polyurethane foam production, were examined. The subjects were followed for 5 yr during which they completed a respiratory symptom questionnaire annually. Pulmonary function and responsiveness to methacholine challenge were measured annually. **toluene** diisocyanate concn in their breathing zones were measured. After the original survey the six subjects were transferred to areas thought to have negligible **toluene** diisocyanate exposures. None of the subjects had respiratory or asthmatic complaints before they started work in polyurethane production. The respiratory symptoms of the subjects did not improve during the followup period. All six had bronchial hyperresponsiveness to methacholine that did not resolve over time. Three subjects demonstrated deficits in 1 second forced expiratory volume of greater than 15% on one of the testing days during the followup period. The need for less or additional asthma therapy of the subjects could not be predicted. The mean time weighted average **toluene** diisocyanate exposure experienced by the subjects was 0.64 ppb; less than 5% of the OSHA standard of 20 ppb. It was concluded that although the outcome of isocyanate induced asthma cannot be predicted, the asthmatic symptoms of these workers have persisted despite the negligible **toluene** diisocyanate exposures.

[Banks DE et al; Chest 97 (1): 121-5 (1990)]**PEER REVIEWED**

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Non-Human Toxicity Excerpts:

THE POSSIBILITY OF DERMAL EXPOSURES TO **TOLUENE** DIISOCYANATE RESULTING IN PULMONARY SENSITIVITY WAS INVESTIGATED USING GUINEA PIGS AS AN ANIMAL MODEL. **TOLUENE** DIISOCYANATE (1-100% CONCN) WAS APPLIED TO DORSAL SITES ON GUINEA PIGS, WHERE SKIN SENSITIVITY TO TDI WAS APPARENT BY THE 7TH DAY. AFTER 14 DAYS, ANIMALS WERE ADDNL EVALUATED FOR TDI SENSITIVITY BY SEROLOGIC ANALYSIS & BRONCHIAL PROVOCATION CHALLENGE. ANTIBODIES TO **TOLUENE** DIISOCYANATE WERE DETECTED USING PASSIVE CUTANEOUS ANAPHYLAXIS, DOUBLE DIFFUSION IN GEL, & RADIOLABELED ANTIGEN BINDING ASSAYS. ANTIBODIES WERE SPECIFIC FOR **TOLUENE** DIISOCYANATE. THE DEVELOPMENT OF RESPIRATORY HYPERSENSITIVITY AS A RESULT OF DERMAL CONTACT WITH **TOLUENE** DIISOCYANATE EMPHASIZES THE IMPORTANCE OF CAREFUL WORKPLACE PRACTICES & SUGGESTS REEVALUATION OF THE ROLE OF INHALATION &/OR DERMAL CONTACT IN CAUSING PULMONARY SENSITIZATION OF WORKERS. [KAROL MH ET AL; TOXICOL APPL PHARMACOL 58 (2): 221 (1981)]**PEER REVIEWED**

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Mechanism of Action:

In order to determine whether treatment with ketotifen inhibits asthmatic reactions induced by **toluene** di-isocyanate, six sensitized subjects with previously demonstrated dual or late asthmatic reaction after inhalation challenge with **toluene** diisocyanate were studied. Ketotifen (1 mg bid, orally) or placebo was administered for 7 days to the examined subjects, according to a double-blind, cross-over, placebo controlled study design. When the subjects were treated with either ketotifen or placebo, forced expiratory volume in 1 second markedly decr after exposure to **toluene** diisocyanate. These results suggest that the anti-asthmatic agent ketotifen is not effective in **toluene** diisocyanate induced asthma and suggest that it should not be used in the prophylaxis of asthmatic reactions induced by **toluene** diisocyanate in sensitized subjects.

[Tossin L et al; Clin Exp Allergy 19 (2): 177-82 (1989)]**PEER REVIEWED**

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Mechanism of Action:

To determine the importance of airway inflammation for the development of late asthmatic reactions, we examined sensitized subjects during late asthmatic reactions induced by exposure to **toluene** diisocyanate in the laboratory. Late asthmatic reactions are associated with a transient increase of bronchial responsiveness and, at the same time, with an increase of neutrophils followed by eosinophils, and of leukotriene B4 and albumin in bronchoalveolar lavage fluid. Late asthmatic reactions, increased bronchial responsiveness, and increase of neutrophils, eosinophils, leukotriene B4, and albumin concn in bronchoalveolar lavage induced by exposure to **toluene** diisocyanate are all prevented by pretreatment with prednisone but not with the nonsteroidal anti-inflammatory agent indomethacin. Aerosolized steroids (beclomethasone and dexamethasone isonicotinate) completely inhibit late asthmatic reactions induced by **toluene** diisocyanate, whereas theophylline has a partial, and verapamil, ketotifen, and cromolyn have no protective effect. These results suggest that late asthmatic reactions induced by **toluene** diisocyanate may be caused by airway inflammation, and that anti-inflammatory steroids should be recommended in the prophylaxis of **toluene** diisocyanate asthma.
[Fabbri LM et al; Am Rev Respir Dis 143 (3 Pt 2): 537-8 (1991)]**PEER REVIEWED**

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Mechanism of Action:

The influence of cyclophosphamide induced granulocyte depletion on **toluene** diisocyanate related changes in airway reactivity and pathology was assessed in guinea pigs. Twelve cyclophosphamide-treated and 12 control animals comprising each group were studied physiologically before and 2 hr after a single 10 min exposure to 3 ppm of **toluene** diisocyanate. Reactivity was determined in intact unanesthetized animals by measuring specific airway conductance before and during intravenous acetylcholine infusion. After testing, tracheal tissue for light microscopic examination was obtained from three hyperreactive guinea pigs in each exposed group and compared with tissue from treated and control animals (n = 3 each) that had not been **toluene** diisocyanate exposed. Cyclophosphamide treatment caused substantial decr in both circulating and airway granulocyte counts. However, the incidence and degree of bronchial hyperreactivity that occurred 2 hr post-**toluene** diisocyanate was similar in the untreated and treated groups. Results indicate that **toluene** diisocyanate induced bronchial hyperreactivity 1) occurs shortly after a brief high concn exposure and 2) appears independent of circulating or airway granulocyte counts.
[Cibulas W Jr et al; J Appl Physiol 64 (5): 1773-8 (1988)]**PEER REVIEWED**

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Mechanism of Action:

A study of the occurrence of serum immunoglobulin-E and immunoglobulin-G antibodies in workers with isocyanate induced asthma was conducted. The study group consisted of 62 workers (58 males) being evaluated for occupational asthma. Thirty nine had been exposed to hexamethylene diisocyanate, 17 to diphenylmethane diisocyanate, and six to **toluene** diisocyanate. The subjects completed a respiratory and occupational questionnaire. Spirometric tests were administered. Skin prick tests were performed with 15 common inhalant allergens and **toluene** diisocyanate, hexamethylene diisocyanate, and diphenylmethane diisocyanate human serum albumin conjugates. Blood samples were collected and assayed for specific serum immunoglobulin-G and immunoglobulin-E antibodies to hexamethylene diisocyanate, diphenylmethan diisocyanate, and **toluene** diisocyanate. Specific inhalation challenges were conducted with hexamethylene diisocyanate, diphenylmethane diisocyanate, and **toluene** diisocyanate. Specific inhalation challenge with **toluene** diisocyanate, hexamethylene diisocyanate, or diphenylmethane diisocyanate induced significant bronchoconstriction in half of the subjects, late reactions being the most common. Twenty subjects had significantly elevated immunoglobulin-G concn and nine had significantly elevated immunoglobulin-G plus immunoglobulin-E concn. Six of 12 subjects with elevated immunoglobulin-E and immunoglobulin-G antibodies had positive skin prick tests for hexamethylene diisocyanate and one was sensitized to diphenylmethane diisocyanate. It was concluded that an association between isocyanate specific antibodies and the results of specific inhalation challenge tests has been established. This suggests that isocyanate induced asthma may involve an immunological mechanism.

[Cartier A et al; J Allergy Clin Immunol 84 (4 Part 1): 507-14 (1989)]**PEER REVIEWED**

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Mechanism of Action:

To investigate the role of pharmacological mechanisms in **toluene** diisocyanate induced occupational asthma, the effects of **toluene** diisocyanate on rat trachea ring and lung parenchymal strip were studied in vitro. The most prominent effect observed was a stimulation of metacholine induced contraction of the tracheal ring by 1M **toluene** diisocyanate (added in dimethyl sulfoxide). The results were less pronounced when **toluene** diisocyanate was added from a stock solution prepared in water, which is possibly due to copolymerisation. It is concluded that the pharmacological effect of **toluene** diisocyanate may result from an autonomic imbalance between cholinergic and B-adrenergic neural control.
[Borm PJA et al; Br J Ind Med 46 (1): 56-9 (1989)]**PEER REVIEWED**

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Mechanism of Action:

SERUM FROM 26 PERSONS SHOWN TO REACT TO PROVOCATIVE INHALATION CHALLENGE WITH LOW CONCN OF **TOLUENE** DIISOCYANATE WAS TESTED BY RADIOALLERGOSORBENT TEST (RAST) USING A P-TOLYL ISOCYANATE-HUMAN SERUM ALBUMIN (TMI-HSA) CONJUGATE. POSITIVE RESULTS WERE OBTAINED IN 15-19% OF **TOLUENE** DIISOCYANATE REACTORS, DEPENDING ON THE METHOD OF EVALUTION. **TOLUENE** DIISOCYANATE ASTHMA MAY BE A COMPLEX SYNDROME WITH SEVERAL TYPES OF REACTIONS POSSIBLE, INCLUDING AN IMMUNOGLOBULIN-E MECHANISM IN SOME INDIVIDUALS. THE THEORY THAT **TOLUENE** DIISOCYANATE ASTHMA IS BASED SOLELY ON AN IMMUNE MECHANISM IS NOT SUPPORTED. THE FINDINGS DO NOT DISAGREE WITH THE HYPOTHESIS THAT **TOLUENE** DIISOCYANATE REACTIVITY MAY BE MEDIATED BY A PHARMACOLOGIC MECHANISM.
[BUTCHER BT ET AL; J ALLERGY CLIN IMMUNOL 66 (3): 213 (1980)]**PEER REVIEWED**

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Mechanism of Action:

Intravenously administered endotoxin inhibits the polymorphonuclear leukocyte dependent airway edema produced in guinea pigs exposed to **toluene** diisocyanate. Tumor necrosis factor is produced in vivo by peripheral blood monocytes and tissue macrophages stimulated with endotoxin and has been shown to activate polymorphonuclear leukocyte's and vascular endothelial cells. To determine whether the inhibition of airway edema is mediated by tumor necrosis factor, guinea pigs were treated with intravenous saline or 75,000 U/kg recombinant human tumor necrosis factor 1.5 hr before exposure to air or 3 ppm **toluene** diisocyanate for 1 hr. Animals were then injected intravenously with 50 mg/kg Evans blue dye as a marker of protein extravasation. Saline-treated animals exposed to **toluene** diisocyanate had a significant increase in tracheal Evans blue dye extravasation (85 + or - 6.5 ug dye/g trachea, mean + or - standard error) compared with saline-treated animals exposed to air (31.3 + or - 2.5, $P < 0.001$). The tracheal extravasation of Evans blue dye was significantly inhibited ($P < 0.05$) in **toluene** diisocyanate exposed animals treated with tumor necrosis factor (64.7 + or - 7.5). Neither heat-inactivated tumor necrosis factor (104.9 + or - 9.5) nor tumor necrosis factor neutralized with a monoclonal antibody against tumor necrosis factor (99.7 + or - 17.9) inhibited **toluene** diisocyanate induced airway edema. In addition, treatment with 15,000 U/kg (99.9 + or - 21.3) or 150,000 U/kg (103.2 + or - 17.6) interleukin 1, a monokine also produced in response to endotoxin, did not prevent airway edema. These results suggest that tumor necrosis factor released in response to endotoxin mediates endotoxin's inhibition of a polymorphonuclear leukocyte dependent airway edema.
[Gordon T, Sheppard D; J Appl Physiol 64 (4): 1988 1688-92]**PEER REVIEWED**

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Mechanism of Action:

Light and electron microscopic structure of lobar bronchial biopsies were examined of nine subjects with occupational asthma induced by **toluene** diisocyanate and of four control nonasthmatic subjects who had never been exposed to **toluene** diisocyanate. Inflammatory cell numbers were separately assessed in the intact epithelium, in the more superficial layer of the submucosa, and in the total submucosa. Asthmatic subjects had an increased number of inflammatory cells in the airway mucosa compared with control subjects. Eosinophils were significantly increased in all compartments, CD45-positive cells were significantly increased in the epithelium and in the more superficial layer of the submucosa, and mast cells were significantly increased only in epithelium. By electron microscopy eosinophils and mast cells appeare degranulated only in asthmatic patients. In the areas of epithelium that appeared intact by light microscopy, electron microscopy showed that, although the intercellular spaces between columnar cells were similar in asthmatic and control groups, the intercellular spaces between basal cells were significantly wider in patients with asthma. Patients with **toluene** diisocyanate induced asthma also had a thicker subepithelial reticular layer, where immunohistochemistry showed the presence of collagen III. In conclusion, in patients with asthma induced by **toluene** diisocyanate, the airway mucosa shows pathologic features, such as inflammatory cell infiltrate and thickening of subepithelial collagen, similar to those described in atopic asthma.
[Saetta M et al; Am Rev Respir Dis 145 (1): 160-8 (1992)]**PEER REVIEWED**

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Probable Routes of Human Exposure:

In a Finnish study, TDI vapor concentrations ranged from 25-80 ug/cu m for pouring, 14-44 ug/cu m for paper stripping, and 1-8 ug/cu m for cutting(1). Personal monitors measured 9-34 ug/cu m and 5-30 ug/cu m of the 2,4-isomer for pouring and paper stripping, respectively(1). While 2,4-**toluene** diisocyanate constitutes 80% of TDI, and 2,6-**toluene** diisocyanate 20%, the 2,4-isomer is more reactive so that the concentration of the 2,6-isomer is higher in workplace air(1). The percentage of 2,4-**toluene** diisocyanate to total **toluene** diisocyanate measured with the personal monitors ranged from 29 to 69%(1). TDI levels of 1.3-2.8 ppb were detected in air inside a Swedish factory manufacturing polyurethanes(2).

[(1) Rosenberg C, Savolainen H; J Chromatography 367: 385-92 (1986) (2) Audunsson G et al; Intern J Environ Anal Chem 20: 85-100 (1985)]**PEER REVIEWED**

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Analytic Laboratory Methods:

A passive monitor for **toluene** diisocyanate which utilizes microporous Teflon diffusion membranes and a 0.5% sulfuric acid absorbing medium was evaluated. The collection rate of **toluene** diisocyanate is proportional to exposure dose from 10 to at least 300 ppb.hr, and response is equivalent for 2,4- and 2,6-**toluene** diisocyanate. Collection rate is independent of humidity and normal atmospheric pressure variations, while temperature causes a decrease of 1.0% per deg C. Negative interference caused by ambient nitrogen dioxide is eliminated by addition of sulfamic acid to the collecting medium. N-Ethylmorpholine is a positive interferent. Field testing of the sampler against a reference impinger technique indicated a positive bias when **toluene** diisocyanate is aerosolized.
[Rando RJ et al; Am Ind Hyg Assoc J 50 (1): 8-14 (1989)]**PEER REVIEWED**

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Environmental Fate/Exposure Summary:

Commercial **toluene** diisocyanate (TDI) is composed of 2 isomers. 2,4-**Toluene** diisocyanate constitutes roughly 80% of TDI, the other 20% being the 2,6-isomer. It may be released to the environment as fugitive emissions and from stack exhaust during the production, transport, and use of TDI in the manufacture of polyurethane foam products and coatings as well as from spills. The types of reactions which the isomers undergo are similar, although the rates may differ. The reactivity of the 2,4-**toluene** diisocyanate with active hydrogen is greater than with the 2,6-isomer, therefore the percentage of 2,4-**toluene** diisocyanate in monitored TDI is generally much less than the 80% in the commercial mixture. However, since much of the monitoring data do not distinguish between isomers, it is not possible to know the proportion of the isomers in the TDI. If spilled on wet land, TDI is rapidly degraded. In one experiment simulating a spill, 5.5% of the original material remained after 24 hours and in a field situation, the concentration of TDI had declined to the ppm levels in 12 weeks. If released into water, a crust forms around the liquid TDI and <0.5% of the original material remains after 35 days. Low concentrations of TDI disappear from the aqueous environment in approximately a day. In the atmosphere, TDI reacts with photochemically produced hydroxyl radicals (half-life 3.3 hr) and is also removed by dry deposition. Human exposure is primarily occupational via inhalation and dermal contact. (SRC)

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Human Toxicity Excerpts:

A survey of the incidence of occupational asthma in a steel coating factory was conducted. The survey was prompted by two male employees developing symptoms suggestive of occupational asthma. The cohort consisted of 221 males employed in the coating shop. A respiratory questionnaire was administered. Spirometric tests were conducted. Peak expiratory flow rate studies were performed on 50 subjects. Twenty one subjects reported symptoms of occupational asthma. Sixty three had other work related symptoms and 58 had respiratory symptoms unrelated to work. The mean length of employment of the subjects with asthmatic symptoms was 7.7 years. All symptomatic subjects had significantly reduced 1 second forced expiratory volumes, compared to asymptomatic workers. 21% of the peak expiratory flow rates were indicative of work related asthma. Two symptomatic subjects were administered inhalation challenge tests with **toluene** diisocyanate after it was discovered that one of the coatings that had been used for 8 years released **toluene** diisocyanate during the coating process. Both subjects showed decreases in forced expiratory volumes of at least 15% below the baseline values. Environmental sampling for **toluene** diisocyanate indicated concentrations ranging from below 0.001 to 0.026 ppm. The coating containing **toluene** diisocyanate was removed from the process. A follow-up survey conducted 1 year later showed that 17 of the symptomatic subjects had become asymptomatic or improved.
[Venables KM et al; Brit J Indus Med 42 (8): 517-24 (1985)]**PEER REVIEWED**

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Human Toxicity Excerpts:

The prevention of airway inflammation caused by **toluene** diisocyanate by prednisone was studied. Healthy **toluene** diisocyanate sensitive individuals were exposed to 0.018 ppm **toluene** diisocyanate in a test chamber. Bronchoalveolar lavage fluid was collected with a flexible fiberoptic bronchoscope. The lavage fluid was spun in a cytocentrifuge and stained with May/Grunwald/Giemsa for differential cell count. The total cell count was performed on resuspended cell pellets. A late asthmatic response was characterized by the occurrence of less than 20% of free expiratory volume in 1 second. The airway responsiveness was assessed by the reaction to methacholine. The cumulative dose of methacholine that produced a 20% decrease in forced expiratory volume in 1 second was used to measure airway responsiveness. Five subjects who received no prednisone treatment developed a late or dual asthmatic reaction. The albumin concn and total number of cells increased in subjects that were given no prednisone compared to controls. There was a significant increase in the number of neutrophils and a small increase in eosinophilia. There was no significant difference in the counts of other cell types. Results suggest that **toluene** diisocyanate induce late asthmatic reactions causing airway inflammation and that prednisone inhibits these reactions.
[Boschetto P et al; J Allergy Clin Immunol 80 (3):261-267 (1987)]**PEER REVIEWED**

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Metabolism/Metabolites:

Epithelial injury and inflammation are involved in airway hyperresponsiveness and asthma induced by **toluene** diisocyanate. In that isocyanates are insoluble and highly reactive compounds, bronchial epithelial cells may represent the most important target cells of their toxic effect. We hypothesized that damage to airway epithelium by **toluene** diisocyanate may result in the release of metabolites of arachidonic acid, which are known to promote inflammation and to alter epithelial cell function and airway smooth muscle responsiveness. To test this hypothesis we examined eicosanoid products in the culture media of bronchial epithelial cells exposed in vitro to 8 and 18 ppb **toluene** diisocyanate. Epithelial cells derived from human bronchi obtained at surgery were cultured to confluency on collagen-coated microporous membranes. Those cells, which expressed differentiated characteristics of epithelial cells (they showed keratin-containing filaments and had a cobblestone appearance), were alternatively exposed to **toluene** diisocyanate or air for 30 min in a specially designed in vitro chamber. The production of metabolites of arachidonic acid was assessed by measuring the release of immunoreactive products into the cell medium at the end of the exposure and during a 2 hr period after exposure. This method revealed a predominant isocyanate induced release of immunoreactive 15-hydroxyeicosatetraenoic acid. Release rate of this compound tended to be dose-related and was associated with cell damage as assessed by the release of lactate dehydrogenase in the medium. [Mattoli S et al; J Cell Physiol 142 (2): 379-85 (1990)]**PEER REVIEWED**

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Emergency Medical Treatment:

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The following Overview, *** **TOLUENE** DIISOCYANATE ***, is relevant for this HSDB record chemical.

Life Support:

- This overview assumes that basic life support measures have been instituted.

Clinical Effects:

SUMMARY OF EXPOSURE

0.2.1.1 ACUTE EXPOSURE

- **Toluene** diisocyanate is an irritant to skin, lungs, conjunctiva and gastrointestinal tract. Euphoria, ataxia, mental aberrations, sensitization (primarily respiratory), bronchitis, emphysema and cor pulmonale can occur.

HEENT

0.2.4.1 ACUTE EXPOSURE

- Severe conjunctival irritation and lacrimation from liquid or high vapor concentrations is likely. Lower concentrations may produce a burning or prickling sensation.
- Glaucoma and iridocyclitis have been reported with a splash accident.

RESPIRATORY

0.2.6.1 ACUTE EXPOSURE

- Burning or irritation of the nose and throat, cough, laryngitis, chest pain, and asthmatic syndrome (chemical bronchitis with severe bronchospasm), sensation of oppression or constriction of the chest, bronchitis, emphysema and cor pulmonale may occur.
- Respiratory symptoms may recur several years after discontinuation of exposure.

NEUROLOGIC

0.2.7.1 ACUTE EXPOSURE

- Acute exposures may produce headache, insomnia, euphoria, ataxia, anxiety neurosis with depression, or paranoid tendencies.

GASTROINTESTINAL

0.2.8.1 ACUTE EXPOSURE

- Inhalation of vapor or aerosol may produce vomiting and abdominal pain. Epigastric and substernal pain may be secondary to the paroxysmal or persistent cough associated with inhalation.

DERMATOLOGIC

0.2.14.1 ACUTE EXPOSURE

- Irritation and inflammation are common. Dermal absorption is low.

IMMUNOLOGIC

0.2.19.1 ACUTE EXPOSURE

- Elevated specific IgE and IgG antibodies have been detected in sensitized and exposed workers. The presence of antibodies does is an indicator of exposure but not of sensitization.

CARCINOGENICITY

0.2.21.1 IARC CATEGORY

- **Toluene** diisocynate has been classified as a 2B agent: possibly carcinogenic to humans, based on sufficient evidence of carcinogenicity in experimental animals and no human data (IARC, 1987).

0.2.21.2 HUMAN OVERVIEW

- **Toluene** diisocyanate is considered a suspected or possible human carcinogen, based on sufficient evidence of carcinogenicity or tumors (spleen, subcutaneous, hepatic, ovarian, peritoneum, mammary gland tissues) in experimental animals (IARC, 1987; US DHHS, 1994; ACGIH, 1995).

Laboratory:

- Monitor respiratory function closely.

Treatment Overview:

ORAL EXPOSURE

- Due to the irritant nature of this substance, emesis is not advised.
- DILUTION: Immediately dilute with 4 to 8 ounces (120 to 240 mL) of milk or water (not to exceed 15 mL/kg in a child).
- ACTIVATED CHARCOAL: Administer charcoal as slurry (240 mL water/30 g charcoal). Usual dose: 25 to 100 g in adults/adolescents, 25 to 50 g in children (1 to 12 years), and 1 g/kg in infants less than 1 year old.
- Monitor patient for respiratory distress. If a cough or difficulty in breathing develops, evaluate for respiratory tract irritation, bronchitis and pneumonia.
- Allergic reaction: Sensitized individuals should be cautioned to avoid further exposure as serious allergic reactions may result.

INHALATION EXPOSURE

- DECONTAMINATION: Move patient to fresh air. Monitor for respiratory distress. If cough or difficulty in breathing develops, evaluate for respiratory tract irritation, bronchitis, or pneumonitis. Administer 100 percent humidified supplemental oxygen with assisted ventilation as required.
- Randomized, double-blind cross-over studies showed minimal efficacy of bronchodilators. This could be due to the absence of airway hyperresponsiveness in some TDI-induced asthma.

EYE EXPOSURE

- DECONTAMINATION: Exposed eyes should be irrigated with copious amounts of tepid water for at least 15 minutes. If irritation, pain, swelling, lacrimation, or photophobia persist, the patient should be seen in a health care facility.

DERMAL EXPOSURE

- DECONTAMINATION: Wash exposed area extremely thoroughly with soap and water. A physician may need to examine the area if irritation or pain persists.

Range of Toxicity:

- Available dose-response information concerning humans pertains to inhalational exposure. Concentrations of 2.5 ppm are considered Immediately Dangerous to Life or Health. A fatality in an asthmatic who continued exposure to TDI has been reported.
- The recommended short term exposure limits for TDI in industry is 0.02 ppm. TDI does not have sufficient warning properties (e.g. odor or eye irritancy) at air concentrations below the recommended short term exposure limit.

[Rumack BH: POISINDEX(R) Information System. Micromedex, Inc., Englewood, CO, 2001; CCIS Volume 107, edition exp February, 2001. Hall AH & Rumack BH (Eds):TOMES(R) Information System. Micromedex, Inc., Englewood, CO, 2001; CCIS Volume 107, edition exp February, 2001.]
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National Toxicology Program Studies:

Groups of 50 female F344/N rats and 50 female B6C3F1 mice were administered commercial grade **toluene** diisocyanate (80% 2,4- and 20% 2,6-) in corn oil by gavage at doses of 60 or 120 mg/kg body weight, 5 days per week for 105 or 106 weeks. Groups of 50 male F344/N rats received 30 or 60 mg/kg and groups of 50 male B6C3F1 mice received 120 or 240 mg/kg on the same schedule. Dosage analyses of **toluene** diisocyanate indicated that the chemical had reacted in the corn oil vehicle, resulting in actual gavage concentrations 77% to 90% of theoretical values. Groups of 50 rats and 50 mice of each sex received corn oil only and served as vehicle controls. Survival in all groups of dosed rats in the 2-year studies was shorter (P less than or equal to 0.005) than that of the controls; depressions in mean body weight gain relative to controls were greater than 10% in all dosed rat groups throughout most of the study. A dose-dependent pattern of cumulative toxicity began at 70 weeks and culminated in excessive mortality, indicating the estimated maximum tolerated dose had been exceeded for rats. Acute bronchopneumonia occurred at increased incidences in groups of dosed male and female rats (males: control, 2/50; low dose, 6/50; high dose, 14/50; females: 1/50, 10/50, 25/49). /Results indicated that/ commercial grade **toluene** diisocyanate in corn oil was carcinogenic for F344/N rats, causing subcutaneous fibromas and fibrosarcomas (combined) in males and females, pancreatic acinar cell adenomas in males, and pancreatic islet cell adenomas, neoplastic nodules of the liver, and mammary gland fibroadenomas in females. **Toluene** diisocyanate was not carcinogenic for male B6C3F1 mice. TDI was carcinogenic for female B6C3F1 mice, causing hemangiomas or hemangiosarcomas (combined), as well as hepatocellular adenomas.
[DHHS/NTP; Toxicology and Carcinogenesis Studies of Commercial Grade 2,4 (80%) and 2,6 (20%) - Toluene Diisocyanate (Gavage Studies) p. 7 (1986) Technical Rpt Series No. 251 NIH Pub No. 86-2507]**PEER REVIEWED**

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Human Toxicity Excerpts:

The importance of airways inflammation for the development of bronchial hyperresponsiveness and for exacerbation of asthma was investigated in subjects with occupational asthma. Subjects sensitized to isocyanates, a small molecular weight compound that causes occupational asthma were examined. Studies in asthmatic subjects sensitized to **toluene** diisocyanate demonstrated that late, but not early, asthmatic reactions induced by **toluene** diisocyanate were associated with an acute increase in bronchial responsiveness, and with a marked infiltration of neutrophils and a slight infiltration of eosinophils into the airways, both prevented by steroids. As the late asthmatic reactions and the increase in responsiveness induced by **toluene** diisocyanate were prevented by steroids, but not by indomethacin, it was speculated that cell membrane phospholipid metabolites, which are inhibited by steroids but not by indomethacin, may be involved in **toluene** diisocyanate induced hyperresponsiveness. The results of these studies suggest that bronchial hyperresponsiveness and exacerbation of asthma may be related to inflammation of the airways and that cell membrane phospholipid metabolites may be involved.
[Mapp CE et al; Bull Eur Physiopathol Respir 23 (6): 583-6 (1987)]**PEER REVIEWED**

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Human Toxicity Excerpts:

Fifty seven polyurethane foam manufacturing workers and 24 reference workers were followed for 4 yr to clarify the effects on pulmonary function of working in polyurethane foam factories with exposure to **toluene** diisocyanate. No significant differences in the average annual losses of pulmonary function for 4 yr were observed among the 28 polyurethane foam workers whose **toluene** diisocyanate exposure levels were very low (mean = 0.1 ppb, group L), the remaining 29 polyurethane foam workers with mean **toluene** diisocyanate exposure of 5.7 ppb (group H), and the reference workers. However, 15 polyurethane foam workers in group H who had experienced peak exposure excursions to 30 ppb or above with a mean concn of 8.2 ppb showed significantly larger average annual losses in percentage maximal mid-expiratory flow, forced expiratory volume in 1 sec ratio to vital capacity, and forced expiratory flow at 25% of forced vital capacity than expected, and significantly larger average annual losses in some obstructive pulmonary function indices than those of the 14 remaining polyurethane foam workers in group H whose peak exposure excursion levels were 3-14 ppb with a mean time-weighted average of 1.7 ppb, group L, and the reference workers. These findings suggest that the peak exposure excursion level of **toluene** diisocyanate might be important in inducing obstructive pulmonary function changes in the polyurethane foam workers rather than the TWA exposure levels, though further comparative studies of the AAL in those who are exposed to different peak exposure excursion levels but the same mean exposure levels are necessary. From the standpoint of prevention, the proposition that peak exposure excursion levels exceeding 20 ppb should be avoided is reasonable.
[Omae K et al; Int Arch Occup Environ Health 63 (8): 565-9 (1992)]**PEER REVIEWED**

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Human Toxicity Excerpts:

The clinical findings and the results of inhalation challenge with **toluene** diisocyanate and methacholine in 113 subjects with a history of exposure to **toluene** diisocyanate and work-related respiratory symptoms are reported. Only some of the subjects (40.7%) had isocyanate asthma, diagnosed by a positive **toluene** diisocyanate inhalation challenge. Most reactors had a dual (30.4%) or a late (41.3%) response. The interval between the last occupational exposure and the specific challenge was significantly shorter in reactors, and among this group the number of immediate reactions to **toluene** diisocyanate decr progressively with an incr interval. The reactors had a significantly higher proportion of positive responses to methacholine and a significantly lower mean PD[1][5] FEV[1] (provocative dose of methacholine which provoked a 15% decrease in forced expiratory volume in 1 second): reactors 557:g, SEM 92.3; non-reactors 1346:g, SEM 128, P < .01. Methacholine challenge could not identify subjects with isocyanate asthma.

[Moscato G et al; J Occup Med 33 (6): 720-5 (1991)]**PEER REVIEWED**

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Human Toxicity Excerpts:

To evaluate the morphologic basis of the different outcomes of **toluene** diisocyanate asthma after quitting occupational exposure, ten patients with **toluene** diisocyanate asthma were examined who showed, at diagnosis, a positive **toluene** diisocyanate challenge test and nonspecific bronchial hyperresponsiveness to methacholine. After diagnosis, all patients ceased work and a 4 to 40 mo follow-up was obtained with three to eight determinations of the cumulative dose producing a 15% fall in forced expiratory volume in 1 second to methacholine in each patient. Bronchoalveolar lavage and biopsy of bronchial muscosa were performed 3 to 39 mo after cessation of work, in the absence of acute exacerbations of the disease. Total cell count in bronchoalveolar lavage fluid was moderately increased in four of ten patients, eosinophils were increased in five of ten patients, and neutrophils were increased in eight of ten patients. Mucosal biopsy specimens of main or lobar bronchi were available in eight of ten patients; epithelial damage and thickening of basement membrane was observed in almost all patients, as well as a mild to moderate inflammatory reaction in the submucosa, mainly represented by lymphocytes, eosinophils, and neutrophils. No relationship was observed between the cellularity of bronchoalveolar lavage and the degree of nonspecific bronchial hyperresponsiveness at the time of bronchoalveolar lavage; mean values of total cells and differential count were not different between patients with presence or absence of the different histologic findings. Mucosal biopsy and bronchoalveolar lavage were performed also in four subjects exposed to dusts without respiratory symptoms or nonspecific bronchial hyperresponsiveness; similar findings were obtained except for the absence of eosinophils in bronchoalveolar lavage and a lesser degree of basement membrane thickening and inflammatory reaction in the submucosa. The study of the changes in nonspecific bronchial hyperresponsiveness after quitting exposure showed that five of ten patients had a significant improvement in nonspecific bronchial hyperresponsiveness to methacholine, as evaluated by a positive significant linear regression between months of work cessation and forced expiratory volume in 1 sec of methacholine; only one of these five patients had an increased number of eosinophils in bronchoalveolar lavage fluid. By contrast, four of the five patients with persistent nonspecific bronchial hyperresponsiveness after quitting exposure had an increased number of eosinophil in bronchoalveolar lavage. It is suggested that persistent nonspecific bronchial hyperresponsiveness in **toluene** diisocyanate asthma after cessation of work may be related to an inflammatory reaction in which eosinophil infiltration seems to be a major determinant.
[Paggiaro P et al; Chest 98 (3): 536-42 (1990)]**PEER REVIEWED**

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Human Toxicity Excerpts:

A 41 yr old automobile paint sprayer showed the clinical features of hypersensitivity pneumonitis 1 wk after he had begun to work with paint materials containing **toluene** diisocyanate. His symptoms began 6 to 8 hr after exposure to the agent and spontaneously disappeared by the next morning. He had diffuse, fine reticulonodular shadows on a chest roentgenogram and a restrictive impairment of pulmonary function. Immunoglobulin G antibody to **toluene** diisocyanate-human serum albumin was present in bronchoalveolar lavage fluid and sera: IgA antibody was present only in bronchoalveolar lavage fluid. Also, the patient had sensitized bronchoalveolar lymphocytes to **toluene** diisocyanate-human serum albumin. The histologic findings suggested hypersensitivity pneumonitis. The results of bronchoalveolar lavage, which was repeated on four separate occasions, showed lymphocytosis and a predominance of suppressor cytotoxic T cells. The findings from serial determinations of humoral antibodies showed no changes consistent with the results of clinical and laboratory studies. In contrast, blastogenic responses of bronchoalveolar lymphocytes to **toluene** diisocyanate markedly decr, and the patient showed clinical improvement despite continued exposure to the agent.
[Yoshizawa Y et al; Ann Intern Med 110 (1): 31-4 (1989)]**PEER REVIEWED**

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Human Toxicity Excerpts:

A case of building related health complaints was investigated with respect to the relationship among frequency of symptoms, antibodies to albumin conjugates of formaldehyde, **toluene** diisocyanate, and trimellitic anhydride, and volatile organic chemicals. The indoor air concn of volatile organic chemicals, formaldehyde, **toluene** diisocyanate and trimellitic anhydride did not exceed Fed-OSHA and ACGIH permissible standards. However, formaldehyde concn ranged between 0.05 and 0.08 ppm. The reported symptoms were multiple, involving the eyes, nose, sinuses, throat, lungs, skeletomuscular system and central nervous system. Anti-formaldehyde, **toluene** diisocyanate, and trimellitic anhydride isotypes were found in 12 of 14 full-time employees and were nondetectable in one part-time employee. The data suggest that a synergistic immunological response to airborne chemicals may be occurring in these subjects. In conclusion, immunological monitoring of affected individuals where chemicals are suspected may prove to be useful in future investigations of building related illness.
[Thrasher JD et al; Am J Ind Med 15 (2): 187-95 (1989)]**PEER REVIEWED**

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Mechanism of Action:

The in vivo exposure to an asthmogenic stimulus, **toluene** diisocyanate, causes airway epithelial damage associated with inflammation and increased bronchial hyperresponsiveness. The latter mechanisms might partly be mediated by the release of eicosanoids from bronchial epithelial cells. Previously it has been demonstrated that the in vitro exposure of bronchial epithelial cells to **toluene** diisocyanate results in the release of immunoreactive 15-hydroxyeicosatetraenoic acid, a product of activation of the 15-lipoxygenase pathway with inflammatory properties. Present study shows that **toluene** diisocyanate induced release of 15-hydroxyeicosatetraenoic acid from epithelial cells can be prevented by nedocromil sodium, an anti-asthmatic drug with anti-inflammatory properties. This mode of action of the compound may explain its clinical effectiveness in asthma.
[Mattoli S et al; Int Arch Allergy Appl Immunol 92 (1): 16-22 (1990)]**PEER REVIEWED**

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Human Toxicity Excerpts:

Thirty factory workers whose annual exposure to **toluene** diisocyanate amounted to 280 hr were examined. Seven of them had been removed from their jobs for presenting respiratory symptomatology and a further five were removed for presenting bronchial asthma. Their medical histories were consulted and further measures were taken such as a radiological thorax study, total immunoglobulin-E, **toluene** diisocyanate, diphenylmethane diisocyanate and hexamethylene diisocyanate RAST, a basal spirometric study and finally a provocation test. The Rast proved negative in every case. In the spirometric study carried out on the provocation test, four cases showed a significant decrease in the forced expiratory volume in 1 second over 20% and over 40% in the FMEF and PEFR. There was no connection between the four patients who presented an elevated total immunoglobulin-E and the four who presented a positive provocation test. The provocation test proved negative in five of the seven patients removed from their places of work. Two of the four workers who responded positively to the provocation test remained in their places of work during the **toluene** diisocyanate foam test without showing any symptoms. The patients who presented symptoms did not appear to present bronchial obstruction during the provocation test. Nonetheless, patients who seemingly had not shown any symptoms presented what appeared to be bronchial obstruction.

[Duce F et al; Allergol Immunopathol (Madr) 16 (3): 139-44 (1988)]**PEER REVIEWED**

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Major Uses:

POLYURETHANE ELASTOMERS MADE FROM **TOLUENE** DIISOCYANATES ARE USED IN COATED FABRICS & CLAY-PIPE SEALS. **TOLUENE** DIISOCYANATES ARE ALSO USED IN ADHESIVES OF POLYURETHANE & OTHER TYPES. /**TOLUENE** DIISOCYANATES/ [IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V19 307 (1979)]**PEER REVIEWED**

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Non-Human Toxicity Excerpts:

In dogs, a correlation has been made between immunological and respiratory responses to **toluene** diisocyanate. Dogs exposed once every second week for 41 wk to 1 mg/kg **toluene** diisocyanate delivered as an aerosol intratracheally developed a systemic immune response to **toluene** diisocyanate conjugated with dog serum albumin as well as immediate-type airway responses.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 307 (1986)]**PEER REVIEWED**

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Human Toxicity Excerpts:

A series of workers with exposure to and respiratory symptoms from **toluene** diisocyanate was compared with a group of exposed, asymptomatic workers and with normal controls using immunologic and clinical evaluations. Improved understanding of **toluene** diisocyanate-induced respiratory disease may best be achieved by categorizing the symptomatic workers into at least 3 and possibly 4 groups: immunologic asthma; pre-existing chronic respiratory disease exacerbated or unaffected by **toluene** diisocyanate; asthma coincidental with exposure, and possibly respiratory disease secondary to toxic or inflammatory mechanisms.
[Patterson R et al; Int Arch Allergy Appl Immunol 84 (1): 93-100 (1987)]**PEER REVIEWED**

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Sediment/Soil Concentrations:

Ten days after an accident resulting in the spillage of 13 tons of **toluene** diisocyanate from a lorry on a swampy wet forest area, **toluene** diisocyanate and toluenediamine were /found/ in the soil. After six yr, only **toluene** diisocyanate-derived polyureas were found in soil samples taken at the same site.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 299 (1986)]**PEER REVIEWED**

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Human Toxicity Excerpts:

The nature of neurohumoral regulation was studied in 125 healthy workers, aged 20-40 yr, with different length of service and **toluene** diisocyanate exposure levels. Adrenal gland activity and some haematological parameters were determined. Neurohumoral regulation of adaptation processes in **toluene** diisocyanate exposed persons seemed to display some cyclicity, somehow related to the length of service. Two early regulatory phases (service up to 3 yr) had common features unrelated to the exposure levels, while after 3 yr of employment some dissimilarities evolved which did depend on the **toluene** diisocyanate exposure levels.
[Ermakova GA, Kryzanovskaja NA; Gigiena truda i Professional'nye Zabolevanija (7): 22-35 (1988)]**PEER REVIEWED**

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NIOSH Recommendations:

Experimental studies have demonstrated that **toluene** and TDA (a hydrolysis product of **toluene** diisocyanate) are carcinogens. The test results meet both OSHA and NIOSH criteria for classifying a substance as a potential occupational carcinogen. NIOSH therefore recommends that all isomers of **toluene** diisocyanate and TDA be considered as potential carcinogens and that exposures be limited to the lowest feasible concn.

[ANON; USDHHS, Public Health Service, Centers for Disease Control, NIOSH, Division of Standards Development and Technology Transfer, 4676 Columbia Parkway, Cincinnati OH 45226, USA, 1989. 20p. Bibl.]**PEER REVIEWED**

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Sampling Procedures:

NIOSH Method: 5521. Analyte: 2,6-**Toluene** diisocyanate. Matrix: Air. Sampler: Impinger (solution of 1-(2-methoxyphenyl)-piperazine in **toluene**). Flow Rate: 1 l/min. Sample Size: 100 liters. Shipment: Ship in screw-cap vial refrigerated @ 4 deg C or lower. Sample Stability: May be unstable; perform steps 8 and 9 as soon as possible. /2,6-**Toluene** diisocyanate/

[U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. 5521-1]**PEER REVIEWED**

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Human Toxicity Excerpts:

Toluene diisocyanate is commonly used as the 2,4 and 2,6 isomers. NIOSH has estimated that 50,000 to 100,000 workers in the United States are regularly exposed to diisocyanates. As of 1977, 49,996 were estimated to be exposed to **toluene** diisocyanate alone. Methods for measuring diisocyanate exposures were considered. The current American Conference of Governmental Industrial Hygienists' recommended standard is 0.005 ppm time weighted average and 0.02 ppm peak for four 15 min periods a day. Results of exposure measurements taken in industry were summarized. Health effects of diisocyanates were discussed. In laboratory animals, **toluene** diisocyanate has caused inflammation and necrosis when applied directly to the skin, conjunctivitis when applied to the eyes, and rhinitis, laryngitis, tracheitis, bronchitis, and pneumonia when inhaled. Diisocyanates are potent pulmonary sensitizers capable of causing isocyanate asthma in humans. They can induce nonspecific airways disease and hypersensitivity pneumonitis after either acute or chronic exposure.
[Musk AW et al; Am J Ind Med 13 (3): 331-49 (1988)]**PEER REVIEWED**

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Human Toxicity Excerpts:

A 46 yr old man who had worked in a paint processing plast for over 29 yr was admitted to our hospital with complaints of nocturnal dyspnea and dry cough. A chest X-ray film showed diffuse granular shadows in bilateral lungs. Pulmonary function tests revealed reduction of diffusing capacity and restrictive impairments. Hypersensitivity pneumonitis due to isocyanates was speculated from his occupational history and clinical course. Positive skin tests against **toluene** diisocyanate-human serum albumin and diphenylmethane diisocyanate-human serum albumin, precipitating antibody against **toluene** diisocyanate-human serum albumin, and negative lymphocyte stimulating tests of peripheral blood and bronchoalveolar lavage fluid were also noticed. Environmental provocation test was positive. Histological findings of transbronchial lung biopsy specimens showed diffuse alveolitis and Masson body, but no granulomas. According to these results, the patient was diagnosed as hypersensitivity pneumonitis due to **toluene** diisocyanate. Type III allergy of Gell-Coombs seems to participate in this case. The granulomatous lesion is seen less frequently in isocyanate related hypersensitivity pneumonitis than in hypersensitivity pneumonitis induced by organic dusts, which suggests the difference in immunological and histological reactions between both types of hypersensitivity pneumonitis.
[Nozawa S et al; Nippon Kyobu Shikkan Gakkai Zasshi 27 (11): 1335-41 (1989)]**PEER REVIEWED**

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Analytic Laboratory Methods:

NIOSH Method: 5521. Analyte: 2,6-**Toluene** diisocyanate. Matrix: Air. Procedure: High performance liquid chromatography, electrochemical and ultra violet detection. For 2,6-**toluene** diisocyanate this method has an estimated detection limit of ca. 0.1 ug diisocyanate/sample. The precision/RSD is not determined and the recovery is not given. Applicability: The working reange is from ug/cu m to more than 1 mg/cu m for a 100 liter air samples. Interferences: Any cmpd which elutes with ureas and absorbs ultraviolet light or is electroactive will interfere with the analysis. /2,6-**Toluene** diisocyanate/ [U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. 5521-1]**PEER REVIEWED**

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Mechanism of Action:

Inhalation of **toluene** diisocyanate results in toxic responses ranging from pulmonary irritation to immunological sensitization. The use of radioactively labeled isocyanate has made it possible to follow the initial uptake of the compound into the bloodstream independent of the final fate of the isocyanate. This study shows that the rate of uptake into the blood is linear during exposure to concn ranging from 0.00005 to 0.146 ppm and that the uptake continues to increase slightly postexposure. It also demonstrates that the radioactivity clears from the bloodstream to a level corresponding to approximately a 100 nM concn of tolyl group after 72 hr and persists at a nanomolar level even 2 wk following the exposure. The initial rate of (14)C uptake is also a linear function of the concn of **toluene** diisocyanate when expressed either as concn (ppm) or as concn multiplied by duration of exposure (ppm.hr). This is discussed in comparison with the toxic responses as a function of both ppm and ppm.hr. Finally, the inclusion of the data on methyl isocyanate indicates that the uptake into arterial blood is a function of exposure concn, independent of isocyanate structure.
[Kennedy AL et al; Toxicol Appl Pharmacol 100 (2): 280-92 (1989)]**PEER REVIEWED**

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Immediately Dangerous to Life or Health:

NIOSH considers 2,4-**toluene** diisocyanate to be a potential occupational carcinogen. /2,4-**Toluene** diisocyanate/

[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

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NIOSH Recommendations:

NIOSH considers 2,4-**toluene** diisocyanate to be a potential occupational carcinogen. /2,4-**Toluene** diisocyanate/

[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

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Environmental Abiotic Degradation:

Toluene diisocyanate reacts readily with compounds containing active hydrogens, such as water, acids, and alcohols(2). Contact with bases may cause uncontrollable polymerization with rapid evolution of heat(2). In concentrated solutions, hydrolysis of one of the isocyanate groups to the amine is followed by rapid reaction of the amine with an isocyanate group on another molecule leading to dimers, oligimers, and polymers(2). In one experiment the hydrolysis product yield was 20% diamine and 80% polyurea(3). When 50 ppm of **toluene** diisocyanate was added to model river and seawater systems, the concn fell to 0.1 ppm or less at the end of 1 day(1).

[(1) Duff PB; The Fate of TDI in the Environment. In: Polyurethane-New Paths to Progress Marketing Technology. Proc. of the SPI 6th Inter. Tech. Marketing Conf. pp. 408-12 (1983) (2) IARC Monograph on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. 39: 287-323 (1985) (3) Sopach ED, Boltromeyuk LP; Gig Sanit 7: 10-3 (1974)]**PEER REVIEWED**

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Sampling Procedures:

A solvent free sampling method for airborne **toluene** diisocyanate was described. Air samples were collected on quartz fiber filters impregnated with 1-(2-methoxyphenyl)piperazine. When the samples were collected on the 1-(2-methoxyphenyl)piperazine coated fibers, the collected **toluene** diisocyanate concn were not affected by changes in relative humidity.
[Robert A, Simon P; Chromatographia 23 (7):507-11 (1987)]**PEER REVIEWED**

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Environmental Biodegradation:

Toluene diisocyanates are expected to be hydrolyzed much more rapidly than they are attacked by microorganisms. The resulting **toluene** diamines are subject to a wide variety of biochemical transformations.

[ITC/USEPA; Information Review #231 (Draft) Toluene Diisocyanates p. 19 (1981)]**PEER REVIEWED**

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Mechanism of Action:

The beta-adrenoceptors on intact peripheral blood lymphocytes were studied in 21 allergic asthmatics, 11 **toluene** diisocyanate asthmatics and 17 normal subjects with radioligand binding assay technique. The airway responsiveness to methacholine provocation test was determined. The results indicated that beta-adrenoceptor Bmax values in allergic and **toluene** diisocyanate asthmatics were reduced but the affinity between receptor and ligand was increased; there was a positive correlation between the values of Bmax and forced expiratory volume in 1 second%, V25/Pr in both asthmatic groups, a positive correlation between the values of Bmax and PC20 in allergic asthmatics. The beta-adrenoceptor responsiveness was remarkably reduced in allergic asthmatics.
[Yang ZF et al; Chin J Tuberc Respir Dis 12 (3): 143-146, 190-191. (1989)]**PEER REVIEWED**

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Non-Human Toxicity Excerpts:

GROUPS OF MALE & FEMALE RATS & MICE WERE EXPOSED TO 0.05 & 0.15 PPM OF 2,4/2,6-**TOLUENE**-DIISOCYANATE (80/20) BY INHALATION FOR 6 HR/DAY, 5 DAYS/WEEK FOR 2 YR. TYPE & INCIDENCE OF TUMORS & THE NUMBER OF TUMOR-BEARING ANIMALS OF EITHER SPECIES DID NOT INDICATE ANY CARCINOGENIC EFFECT. HEMATOLOGY, BIOCHEMISTRY, URINALYSIS, & CYTOGENICITY STUDIES DID NOT REVEAL ANY UNTOWARD EFFECT. INCREASED MORTALITY (FEMALES ONLY), REDUCED WEIGHT GAIN & SIGNS OF IRRITATION IN THE UPPER & LOWER RESPIRATORY TRACT RESULTED FROM EXPOSURE TO **TOLUENE** DIISOCYANATE IN THE MOUSE STUDY WITH THE HIGHEST INCIDENCE IN THE 0.15 PPM EXPOSURE LEVEL.
[LOESER E; TOXICOL LETT (AMST) 71 (1983)]**PEER REVIEWED**

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Human Toxicity Excerpts:

The respiratory status of factory workers exposed continously to isocyanates over 10 years was studied. A total of 80 workers in two facilities that manufactured fixtures used in the interiors of cars were examined and underwent spirometry before and after work. Of these, 12 were comparisons not exposed to **toluene** diisocyanate. Subjects included those previously examined in 1971. Ventilatory capacity tests were performed inlcuding forced expiratory volume in 1 sec and forced vital capacity testing. Annual decrements were calculated. The mean average concentration of **toluene** diisocyanate was not more than 0.0033 ppm respectively. Subjects who had been studied previously had a mean forced vital capacity of 104.6% and a mean forced expiratory volume in 1 sec of 107% of predicted values. Three subjects with significant obstruction in the lung function tests were smokers. The comparisons in facility 1 had a significantly lower percentage of the predicted forced fital capacity and forced expiratory volume than the exposed population. Most of the data from 1971 for annual decrement calculations were not reliable. A 10% decrement in forced vital capacity and forced expiratory volume in 1 second was indicative of significant postshift decline and would indicate the presence of isocyanate asthma or hypersensitivity; no subject at either facility met the criteria.
[Gee JB; Morgan WKC; J Occup Med 27 (1): 15-8 (1985)]**PEER REVIEWED**

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Human Toxicity Excerpts:

Amine induced asthma was studied in polyurethane foam workers. A total of 12 subjects, occupationally exposed to polyurethane foams, who complained of wheezing and breathlessness at work were tested. Subjects were given 20 to 2000 ug methacholine. Forced expiratory volume in 1 sec was measured. Subjects were challenged with 0.01 ppm **toluene** diisocyanate for 15 min in an atmosphere chamber. Forced expiratory volume in 1 sec was measured. Positive tests were considered as a 15% fall in forced expiratory volume in 1 sec. High sensitivity to methacholine was seen in ten subjects with a 15% fall in forced expiratory volume in 1 sec at <1000 ug; normal subjects responded at 2000 ug. All subjects reacted to **toluene** diisocyanate.
[Cardura F, Moscata G; Brit J Indus Med 41: 552-3 (1984)]**PEER REVIEWED**

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Human Toxicity Excerpts:

Sensitized subjects may develop symptoms of asthma after exposure to isocyanates in their place of work. After challenge with isocyanates in the laboratory, sensitized subjects develop immediate, late and dual asthmatic reactions. **Toluene** diisocyanate might cause late asthmatic reactions and increase bronchial responsiveness by causing an acute inflammatory reaction in the airways, and that airway inflammation may be responsible for persistence of occupational asthma induced by isocyanates. To test these hypotheses, sensitized subjects were examined during asthmatic reactions induced by exposure to **toluene** diisocyanate in the laboratory. It was observed that late and dual, but not early, asthmatic reactions are associated with a transient increase of bronchial responsiveness which is associated with an acute inflammatory reaction of the airways characterized by an increase of neutrophils followed by eosinophils, by an increase of leukotriene B4 and albumin in bronchoalveolar lavage fluid, and that all these effects are inhibited by steroids. Longitudinal studies suggest that the majority of subjects with occupational asthma continue to have persistent asthma months and yrs after the cessation of exposure, and the results of our studies combined with the results of studies performed by others suggest that the persistence of asthma may be related to the persistence of airway inflammation.
[Fabbri LM et al; Eur Respir J (Suppl 13): 136-38 (1991)]**PEER REVIEWED**

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Human Toxicity Excerpts:

Twelve subjects were studied with inhalation challenge testing to **toluene** diisocyanate because of suspected asthma based on a consistent clinical and occupational history. In seven cases, asthma was documented by a positive inhalation challenge to low levels of **toluene** diisocyanate. Six of the seven reactors had persistent respiratory symptoms and required daily treatment even though they had been removed from isocyanate exposure for intervals as long as 12 years (mean 4.5 years). These six reactors had either dual (four cases) or late bronchospasm (two cases) to less than 20 ppb and all had a positive methacholine or cold air challenge prior to study. The one reactor with a negative methacholine challenge had a positive (immediate) bronchospastic response to a challenge performed one week after removal from isocyanate exposure. Five workers had a negative challenge, two of whom had persistent respiratory symptoms and positive methacholine challenges at the time of inhalation testing. ... Respiratory symptoms may persist following long-term removal from occupational exposure to and are associated with nonspecific bronchial hyperreactivity. The sensitivity may also persist for a long time even in the absence of any additional occupational exposure. Long-term prospective studies of symptomatic isocyanate workers are needed to fully define the extent of this problem.
[Moller DR et al; Chest 90 (4): 499 (1986)]**PEER REVIEWED**

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Protective Equipment & Clothing:

Recommendations for respirator selection: Condition: At concentrations above the NIOSH REL, or where there is no REL, at any detectable concentration: Respirator Class(es): Any self-contained breathing apparatus that has a full facepiece and is operated in a pressure-demand or other positive pressure-mode. Any supplied-air respirator that has a full facepiece and is operated in a pressure-demand or other positive-pressure mode in combination with an auxiliary self-contained breathing apparatus operated in pressure-demand or other positive-pressure mode. /**Toluene** 2,4-diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

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Protective Equipment & Clothing:

Facilities for quickly drenching the body should be provided within the immediate work area for emergency use where there is a possibility of exposure. (Note: It is intended that these facilities provide a sufficient quantity or flow of water to quickly remove the substance from any body areas likely to be exposed. The actual determination of what constitutes an adequate quick drench facility depends on the specific circumstances. In certain instances, a deluge shower should be readily available, whereas in others, the availability of water from a sink or hose could be considered adequate.) /**Toluene** 2,4-diisocyanate/

[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

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Protective Equipment & Clothing:

Eyewash fountains should be provided in areas where there is any possibility that workers could be exposed to the substance; this is irrespective of the recommendation involving the wearing of eye protection. /**Toluene** 2,4-diisocyanate/

[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

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Protective Equipment & Clothing:

Wear appropriate personal protective clothing to prevent skin contact. /**Toluene** 2,4-diisocyanate/ [NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

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Protective Equipment & Clothing:

Wear appropriate eye protection to prevent eye contact. /**Toluene** 2,4-diisocyanate/ [NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

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Skin, Eye and Respiratory Irritations:

AS A VAPOR ... /**TOLUENE** DIISOCYANATE/ IS A POWERFUL IRRITANT TO EYES, SKIN, RESPIRATORY TRACT.
[Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984.,p. II-414]**PEER REVIEWED**

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Hazardous Reactivities & Incompatibilities:

Strong oxidizers, water, acids, bases and amines (may cause foam and splatter); alcohols. [Note: Reacts slowly with water to form carbon dioxide and polyureas.] /**Toluene** 2,4-diisocyanate/

[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

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U. S. Exports:

(1984) 6.27x10+10 g /**TOLUENE** DIISOCYANATES/
[BUREAU OF THE CENSUS. U.S. EXPORTS (1984) p.2-73]**PEER REVIEWED**

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Consumption Patterns:

CHEMICAL PROFILE: **Toluene** diisocyanate. Demand: 1986: 650 million lb; 1987: 695 million lb; 1991 /projected/: 720 million lb (Includes exports, imports are negligible).
[Kavaler AR; Chemical Marketing Reporter 232 (25): 50 (1987)]**PEER REVIEWED**

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Odor Threshold:

TOLUENE DIISOCYANATE HAS MARKED CHARACTERISTIC ODOR WHICH ALLOWS IT TO BE DETECTED READILY. YET @ MAX RECOMMENDED CONCN (0.02 PPM) THE POISON CANNOT BE DETECTED BY ITS SMELL.

[Lefaux, R. Practical Toxicology of Plastics. Cleveland: CRC Press Inc., 1968. 102]**PEER REVIEWED**

TOLUENE DIISOCYANATE

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Consumption Patterns:

CHEMICAL PROFILE: **Toluene** Diisocyanate. Flexible urethane foams, 65%; (furniture, 28%; transportation, 16%; carpet underlay, 9%; bedding, 6%; other foam uses, 6%;) exports, 22%; rigid foams, 5%; polyurethane coatings, 4%; elastomers, 2%; miscellaneous non-foam uses, 2%.
[Kavaler AR; Chemical Marketing Reporter 232 (25): 50 (1987)]**PEER REVIEWED**

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Manufacturers:

Olin Corporation, 120 Long Ridge Road, Stamford, CT 06904, (203) 356-2000 /**Toluene** 2,4- and 2,6-diisocyanate (80/20) mixture/

[United States International Trade Commission. Synthetic Organic Chemicals-United States Production and Sales, 1991. USITC Publication 2607, February 1993.Washington, DC: United States Trade Commission, 1993.,p. 3-8]**PEER REVIEWED**

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Preventive Measures:

The worker should immediately wash the skin when it becomes contaminated. /**Toluene** 2,4-diisocyanate/

[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

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Preventive Measures:

The worker should wash daily at the end of each work shift. /**Toluene** 2,4-diisocyanate/ [NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

TOLUENE DIISOCYANATE

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Preventive Measures:

Work clothing that becomes wet or significantly contaminated should be removed and replaced. /**Toluene** 2,4-diisocyanate/

[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

TOLUENE DIISOCYANATE

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Preventive Measures:

Workers whose clothing may have become contaminated should change into uncontaminated clothing before leaving the work premises. /**Toluene** 2,4-diisocyanate/

[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

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Manufacturers:

Dow Chemical Co, 2020 Willard H. Dow Center, Midland, MI 48674, (517) 636-6125 /**Toluene** 2,4- and 2,6-diisocyanate (80/20) mixture/

[United States International Trade Commission. Synthetic Organic Chemicals-United States Production and Sales, 1991. USITC Publication 2607, February 1993.Washington, DC: United States Trade Commission, 1993.,p. 3-8]**PEER REVIEWED**

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Manufacturers:

ICI Americas, Inc., Polyurethane Group 286 Manuta Grove Road, W. Deptford, NJ 08066-1732. (609) 423-8300; Speciality Product Division Concord Pike & Murphy Rd, Willmington, DE 19897, (302) 886-3000 /**Toluene** 2,4- and 2,6-diisocyanate (80/20) mixture/

[United States International Trade Commission. Synthetic Organic Chemicals-United States Production and Sales, 1991. USITC Publication 2607, February 1993.Washington, DC: United States Trade Commission, 1993.,p. 3-8]**PEER REVIEWED**

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Manufacturers:

BASF Corporation, Chemicals Division, 1255 Broad St., Cliftn, NJ 07015, (201) 316-2937 /**Toluene** 2,4- and 2,6-diiscyanate (80/20) mixture/

[United States International Trade Commission. Synthetic Organic Chemicals-United States Production and Sales, 1991. USITC Publication 2607, February 1993.Washington, DC: United States Trade Commission, 1993.,p. 3-8]**PEER REVIEWED**

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Methods of Manufacturing:

From **toluene** diamine by reaction with carbonyl chloride (phosgene)
[Zenz, C. Occupational Medicine-Principles and Practical Applications. 2nd ed. St. Louis, MO: Mosby-Yearbook, Inc, 1988. 1016]**PEER REVIEWED**

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Major Uses:

POLYURETHANE COATINGS MADE FROM **TOLUENE** DIISOCYANATE MIXT ... IN GENERAL ... ARE USED IN FLOOR FINISHES, WOOD FINISHES & SEALERS, TRADE SALES PAINTS, CONCRETE SEALERS, & IN COATINGS FOR AIRCRAFT, TANK TRUCKS, TRUCK TRAILERS & TRUCK FLEETS. /MIXT OF 2,4- & 2,6-ISOMERS/
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V19 307 (1979)]**PEER REVIEWED**

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Protective Equipment & Clothing:

Recommendations for respirator selection: Escape from suddenly occurring respiratory hazards: Respirator Class(es): Any air-purifying, full-facepiece respirator (gas mask) with a chin-style, front- or back-mounted organic vapor canister. Any appropriate escape-type, self-contained breathing apparatus. /**Toluene** 2,4-diisocyanate/

[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

TOLUENE DIISOCYANATE

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Manufacturers:

Rubicon, Inc, PO Box 517, Geismar, LA 70734, (504) 673-6141 /**Toluene** 2,4- and 2,6-diisocyanate (80/20) mixture/

[United States International Trade Commission. Synthetic Organic Chemicals-United States Production and Sales, 1991. USITC Publication 2607, February 1993.Washington, DC: United States Trade Commission, 1993.,p. 3-8]**PEER REVIEWED**

TOLUENE DIISOCYANATE

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Methods of Manufacturing:

NITRATION OF **TOLUENE**, FOLLOWED BY REDUCTION TO DIAMINE, REACTION WITH PHOSGENE, PURIFICATION, AND RECOVERY OF COPRODUCT HYDROGEN CHLORIDE.
[CHEM & ENG NEWS 63 (37): 16 (1985)]**PEER REVIEWED**

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Fire Potential:

DUE TO ITS HIGH FLASH POINT, **TOLUENE** DIISOCYANATE OFFERS NO SERIOUS RISK OF FIRE ... .

[Lefaux, R. Practical Toxicology of Plastics. Cleveland: CRC Press Inc., 1968. 103]**PEER REVIEWED**

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Human Toxicity Excerpts:

Symptoms and lung function of workers exposed to isocyanates in polyurethane foam factories were studied. A group of 67 workers was examined for **toluene**-diisocyanate ... exposure. Measurements were made by samples obtained from subject carried pumps. Interviews were also conducted for information of symptoms involving the nose, eyes, upper airways, and lung. Another group of 56 nonexposed workers was determined by spirometry and nitrogen wash out prior to the work shift. The exposed workers were examined again immediately after work. The variables studied were forced expired vital capacity and forced expired volume in 1 second. ... The highest exposure group was foaming machine workers, with a day mean exposure of 0.023 mg/cu m. Nonsmokers showed an increased frequency of symptoms involving the nose, throat, and dyspnea. Smokers had no significant increase. Smokers of the exposed group reported coughing. Only smokers reported symptoms classified as chronic bronchitis, with frequency independent of exposure. Decreased forced expired vital capacity and forced expired volume were observed in the exposed group. This group also showed increased expired vital capacity. Lung function impairment was restricted to smokers. Spirometric and nitrogen washout variables did not change significantly during the work shift. Decreasing spirometric values with increased exposure was seen in smokers. Conclusions indicate that mean exposure of 0.01 mg/cu m/day to isocyanates may give an increased frequency of symptoms in nonsmokers.
[Alexanderson R et al; Internat Archives of Occup Environ Health 55 (2): 149-57 (1985)]**PEER REVIEWED**

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Special Reports:

Kay S; Food and Chemical Toxicology 23 (3): 411-13. (1985) **Toluene** diisocyanate and Lung Function.

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Analytic Laboratory Methods:

DETERMINATION OF **TOLUENE** DIISOCYANATE (TDI) IN AIR BY LC. MAX SENSITIVITY IS OBSERVED AT AN EXCITATION WAVELENGTH OF 226 NM & USING A 300-NM CUT-OFF EMISSION FILTER. A DETECTION LIMIT OF 0.4 PPB FOR TDI CAN BE ACHIEVED WITH A 1 L AIR SAMPLE.
[KORMOS LH ET AL; ANAL CHEM 53 (7): 1122 (1981)]**PEER REVIEWED**

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Disposal Methods:

Toluene diisocyanate is a waste chemical stream constituent which may be subjected to ultimate disposal by controlled incineration. Controlled incineration: Oxides of nitrogen are removed from the effluent gas by scrubbers and/or thermal devices.
[USEPA; Engineering Handbook for Hazardous Waste Incineration p.2-10 (1981) EPA 68-03-3025]**PEER REVIEWED**

TOLUENE DIISOCYANATE

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Analytic Laboratory Methods:

GASES IN THE ATMOSPHERE ARE MONITORED WITH CHEMICALLY-COATED QUARTZ PIEZOELECTRIC CRYSTALS; THE METHOD IS DEMONSTRATED IN THE USE OF POLYETHYLENE GLYCOL FOR **TOLUENE** DIISOCYANATE DETERMINATION. A MICROPROCESSOR IS USED TO CONTROL THE GAS SAMPLE FLOW THROUGH THE DETECTOR HEAD AS WELL AS THE DATA ACQUISITION. THE THEORETICAL DETECTION LIMIT IS APPROX 0.006 PPM.
[ALDER JF, ISAAC CA; ANAL CHIM ACTA 129 (1): 175 (1981)]**PEER REVIEWED**

TOLUENE DIISOCYANATE

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Analytic Laboratory Methods:

DETERMINATION OF **TOLUENE** DIISOCYANATE WORKING ATMOSPHERES BY HPLC USING UV OR FLUORESCENCE DETECTION. THE DETECTION LIMIT IS APPROX 1X10-4 MG/CU M.
[SANGOE C, ZIMERSON E; J LIQ CHROMATOGR 3 (7): 971 (1980)]**PEER REVIEWED**

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Non-Human Toxicity Excerpts:

Rats receiving up to 240 mg/kg **toluene** diisocyanate by gavage daily on 5 days/wk for 13 wk were found to suffer from mild to moderate bronchopneumonia.

[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 306 (1986)]**PEER REVIEWED**

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Sampling Procedures:

EPA Method 8020. For the analysis of solid waste, a representative sample (solid or liquid) is collected in a standard 40 ml glass screw cap VOA vial equipped with a Teflon faced silicone septum. Sample agitation, as well as contamination of the sample with air, must be avoided. Two vials are filled per sample location, then placed in separate plastic bags for shipment and storage. /**Toluene**/ [USEPA; Test Methods for Evaluating Solid Waste SW-846 (1986)]**PEER REVIEWED**

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Non-Human Toxicity Excerpts:

Groups of 120 male and 120 female CD-1 mice, three to four weeks old, were exposed to 0, 0.05, or 0.15 ppm (0, 0.36 or 1.07 mg/cu m) production grade **toluene** diisocyanate (approx 80% 2,4 isomer & 20% 2,6 isomer) in an inhalation chamber for 6 hr/day on 5 days/wk for 104 wk. There was a significant reduction in body weight in the high-dose group /sex not stated/ and a significant increase in mortality in both high and low-dose females by the termination of the study. No such effect was seen in males. Neither the types of tumor observed nor their incidences were dose-related, and both corresponded to those seen in historical controls for this strain of mice. However, dose-related pathological changes were observed in the nasal cavity (chronic or necrotic rhinitis), together with changes in the lower respiratory tract (interstitial pneumonia, catarrhal bronchitis) in both groups.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 303 (1986)]**PEER REVIEWED**

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Non-Human Toxicity Excerpts:

Groups of 126 male and 126 female Sprague Dawley CD rats, six to nine weeks old, were exposed to 0, 0.05 or 0.15 ppm (0, 0.36 or 1.07 mg/cu m) production-grade **toluene** diisocyanate (approx 80% 2,4 isomer and 20% 2,6 isomer) in an inhalation chamber for 6 hr/day on 5 days/wk for 108 wk or 110 wk. A significant reduction in weight gain was observed during the first 12 wk of the study among the high-dose animals of each sex, but body wt gain was similar in all groups thereafter. No significant difference in mortality between treated and control groups of either sex was reported. Tumor incidences and types were reported to be similar in control and treated groups.

[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 304 (1986)]**PEER REVIEWED**

TOLUENE DIISOCYANATE

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NIOSH Recommendations:

NIOSH usually recommends that occupational exposures to carcinogens be limited to the lowest feasible concentration. /2,4-**Toluene** diisocyanate/

[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

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Probable Routes of Human Exposure:

THE RESPIRATORY HEALTH OF 277 WORKERS IN A NEW **TOLUENE** DIISOCYANATE (TDI) MANUFACTURING PLANT WAS STUDIED PROSPECTIVELY DURING 5 YR OF EXPOSURE. PERSONAL TDI MONITORS WERE USED TO CONTINUOUSLY MEASURE PEAK & 8-HR TIME-WEIGHTED AVG (TWA) CONCN IN MORE THAN 2000 SAMPLES. REGRESSION OF ANNUAL CHANGE ON SMOKING (PACK-YEARS), ATOPIC STATUS & CUMULATIVE TDI EXPOSURE, DICHOTOMIZED AT 68.2 PPB MONTHS INTO LOW & HIGH EXPOSURE GROUPS, SHOWED SIGNIFICANT EFFECTS OF SMOKING ON SPIROMETRIC TESTS & LUNG VOLUMES. AFTER ADJUSTING FOR PACK-YEARS OF SMOKING, THE 74 MEN IN THE HIGH CUMULATIVE TDI EXPOSURE CATEGORY HAD SIGNIFICANTLY LARGER DECLINE IN FEV1 (1-S FORCED EXPIRATORY VOLUME), % FEV (% FORCED EXPIRATORY VOLUME) & FEF25-75% (FORCED EXPIRATORY FRACTION FROM 25 TO 75% VITAL CAPACITY) THAN DID THE 149 MEN IN THE LOW CATEGORY. ANNUAL CHANGE IN FEV1 WAS THEN EXAMINED IN 6 SMOKING-EXPOSURE CATEGORIES: IN NEVER-SMOKERS, AVG ANNUAL DECLINE WAS 38 ML/YR GREATER IN THOSE WITH HIGHER CUMULATIVE TDI EXPOSURE.
[DIEM JE ET AL; AM REV RESPIR DIS 126 (3): 420 (1982)]**PEER REVIEWED**

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Probable Routes of Human Exposure:

Exposure to **toluene** diisocyanate is primarily occupational via inhalation or dermal contact with the aerosol or vapor. Workers may also be exposed through skin contact with freshly cured foam or as a result of spills or splashes. (SRC)

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Natural Pollution Sources:

2,4- and 2,6-**toluene** diisocyanate, the components of commercial TDI are not known to occur as a natural product(1).

[(1) IARC; Monograph on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. 19: 303-11 (1979)]**PEER REVIEWED**

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Human Toxicity Excerpts:

A shortened protocol was developed for the epidemiological measurement of bronchial responsiveness to methacholine without compromising sensitivity, power, precision or safety, and without distorting the numerical value of the PD20.FEV1 (the cumulative dose from a doubling incremental sequence which provokes a 20% decrement in forced expiratory volume in 1 second). It was used in a survey of 254 polyurethane workers (83% of the eligible workforce) exposed occupationally to **toluene** diisocyanate. The mean duration of each test proved to be 38 min, it was well tolerated and 64 workers (25%) proved to be reactors. PD20.FEV1 appeared to be distributed unimodally. It was significantly correlated with questionnaire records of shortness of breath, chest tightness, and wheeze; and with pre-shift forced expiratory volume in 1 second and FEF25-75. Even the reactors requiring the highest dose of 640 cumulative inhalation units (1 unit = one 8.9 ul inhalation of methacholine 1 mg/ml) to generate a PD20 measurement reported significantly more wheeze than the non-reactors. This indicates that the test had clinical meaning throughout its dose range of 0.3-640 units. No correlation was found between PD20 and individual changes in ventilatory function across the working shift, but mean shift changes were negligible and not statistically significant. PD20 was also found to be unrelated to age, sex, race, smoking, cough and atopy.
[Hendrick DJ; Bull Eur Physiopathol Respir 23 (6): 555-9 (1987)]**PEER REVIEWED**

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Analytic Laboratory Methods:

Isocyanate determination air paper tape Hydrazine determination air paper tape;Air analysis Hydrazine deriv. and **toluene** diisocyanate determination. in, miniature paper tape apparatus for
[Hughes WT Jr; Anal Instrum (Research Triangle Park, N. C.) 22: 87-98 (1986)]**PEER REVIEWED**

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Non-Human Toxicity Excerpts:

Toluene diisocyanate was mutagenic in Salmonella typhimurium strains TA98 and TA100 in the presence (but not the absence) of Aroclor 1254-induced male Sprague Dawley rat or male Syrian hamster liver S9; it was not mutagenic in strains TA 1535 or 1537.
[DHHS/NTP; Toxicology and Carcinogenesis Studies of Commercial Grade 2,4 (80%) and 2,6 (20%) - Toluene Diisocyanate (Gavage Studies) p. 7 (1986) Technical Rpt Series No. 251 NIH Pub No. 86-2507]**PEER REVIEWED**

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Medical Surveillance:

A SCREENING PROGRAM WAS UNDERTAKEN AT A RESEARCH & DEVELOPMENT FACILITY OF A LARGE **TOLUENE**-DIISOCYANATE (TDI) MANUFACTURING CORPORATION. THE PURPOSE WAS TO DETERMINE THE OCCURRENCE OF ANTIBODIES TO TDI IN SELECTED WORKER POPULATIONS. NO TOLYL-REACTIVE IMMUNOGLOBULIN-E ANTIBODIES WERE DETECTED IN SERA WHEN WORKERS WERE EXPOSED ONLY TO AMBIENT TDI CONCN. WORKERS HAD ACUTE EXPOSURES TO TDI AS A RESULT OF SPILLS OR SPLASHES. ANTIBODY RESPONSES DEVELOPED IN 3 OF 4 INDIVIDUALS WHOSE ACUTE EXPOSURES WERE ACCOMPANIED BY IMMEDIATE RESPIRATORY SYMPTOMATOLOGY & A DECREASED FORCED EXPIRATORY VOLUME. AN ANTIBODY RESPONSE DEVELOPED IN 1 OF 9 WORKERS & IMMEDIATE RESPIRATORY SYMPTOMS, BUT NO SPIROMETRIC CHANGES UPON ACUTE TDI EXPOSURE. ROUTINE SEROLOGIC SCREENING OF WORKERS FOR TOLYL-REACTIVE ANTIBODIES MAY BE OF VALUE IN CONFIRMING SUSPECTED ISOCYANATE EXPOSURE & IN PROVIDING AN EARLY WARNING OF DEVELOPING TDI HYPERSENSITIVITY.
[KAROL MH; J OCCUP MED 23 (11): 741 (1981)]**PEER REVIEWED**

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Sampling Procedures:

NIOSH Method: 5505. Analyte: 1-(2-methoxyphenyl)piperazine; HCO group. Matrix: Air. Sampler: Impinger (solution of 1-(2-methoxyphenyl)-piperazine in **toluene**). Flow Rate: 1 l/min. Sample Size: 600 liters. Shipment: In vials; flammable liquid. Sample Stability: Equal to or greater than 2 weeks. /Isocyanate group/

[U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. 5505-1]**PEER REVIEWED**

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Medical Surveillance:

/Protect/ from exposure those individuals with diseases of blood and liver. Physical exam of exposed personnel annually, incl blood count and liver functions. /**Toluene**-2,4-diisocyanate/

[ITII. Toxic and Hazardous Industrial Chemicals Safety Manual. Tokyo, Japan: The International Technical Information Institute, 1988. 528]**PEER REVIEWED**

TOLUENE DIISOCYANATE

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Analytic Laboratory Methods:

TOLUENE DIISOCYANATE ... DETERMINED IN ... ATMOSPHERE BY TLC.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V19 309 (1979)]**PEER REVIEWED**

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RCRA Requirements:

U223; As stipulated in 40 CFR 261.33, when **toluene** diisocyanate, as a commercial chemical product or manufacturing chemical intermediate or an off-specification commercial chemical product or a manufacturing chemical intermediate, becomes a waste, it must be managed according to Federal and/or State hazardous waste regulations. Also defined as a hazardous waste is any residue, contaminated soil, water, or other debris resulting from the cleanup of a spill, into water or on dry land, of this waste. Generators of small quantities of this waste may qualify for partial exclusion from hazardous waste regulations (40 CFR 261.5).

[40 CFR 261.33 (7/1/91)]**PEER REVIEWED**

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Human Toxicity Excerpts:

TOLUENE DIISOCYANATE (TDI) SENSITIVITY ACCOMPANIED BY NONSPECIFIC BRONCHIAL HYPERRESPONSIVENESS OCCURS IN 5% OF OCCUPATIONALLY EXPOSED WORKERS. THE CASE OF A 32 YR OLD WORKER FOLLOWED LONGITUDINALLY AFTER REMOVAL FROM ISOCYANATE EXPOSURE IS REPORTED. TDI REACTIVITY WAS LOST 11 MONTHS AFTER REMOVAL FROM EXPOSURE & NONSPECIFIC BRONCHIAL HYPERRESPONSIVENESS RESOLVED AFTER 17 MONTHS. IMMUNOPHARMACOLOGIC RESULTS SHOW THAT THE WORKER'S INITIAL DECREASED ABILITY OF LYMPHOCYTES TO PRODUCE CYCLIC-AMP RETURNED TO NEAR NORMAL AFTER 2 YR. IMMUNOGLOBULIN-E ANTIBODIES TO A HUMAN SERUM ALBUMIN TOLYL MONOISOCYANATE CONJUGATE WERE STILL PRESENT THIS TIME.
[BUTCHER BT ET AL; J ALLERGY CLIN IMMUNOL 70 (4): 231 (1982)]**PEER REVIEWED**

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Atmospheric Standards:

This action promulgates standards of performance for equipment leaks of Volatile Organic Compounds (VOC) in the Synthetic Organic Chemical Manufacturing Industry (SOCMI). The intended effect of these standards is to require all newly constructed, modified, and reconstructed SOCMI process units to use the best demonstrated system of continuous emission reduction for equipment leaks of VOC, considering costs, non air quality health and environmental impact and energy requirements. **Toluene** diisocyanate is produced, as an intermediate or a final product, by process units covered under this subpart.

[40 CFR 60.489 (7/1/91)]**PEER REVIEWED**

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Probable Routes of Human Exposure:

Concentration medians for 2,4-**toluene** diisocyanate in 2 plants producing flexible polyurethane foam were 0.70 and 0.33 ppb for the mixing and finishing ends, respectively(1). The respective median values for 2,6-TDI were 0.91 and 1.1 ppb. Maximum concentrations of 2,6-TDI exceeded 64 ppb at the finishing end(1).

[(1) Rando RJ et al; Am Ind Hyg Assoc J 45: 199-203 (1984)]**PEER REVIEWED**

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Non-Human Toxicity Excerpts:

TOLUENE DIISOCYANATE WAS MUTAGENIC IN SALMONELLA TYPHIMURIUM STRAINS TA1538 & TA98 AFTER METABOLIC ACTIVATION.
[ANDERSEN M ET AL; SCAND J WORK ENVIRON HEALTH 6 (3): 221 (1980)]**PEER REVIEWED**

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Artificial Pollution Sources:

Levels of 100-17,700 ug/cu m **toluene** diisocyanate were reported in samples from the stack exhaust of a polyurethane foam production plant.

[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 299 (1986)]**PEER REVIEWED**

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Mechanism of Action:

Serum immunoglobulin-G and immunoglobulin-E to isocyanate haptenized human serum albumin (HSA) were estimated by ELISA in 55 isocyanate workers who underwent isocyanate inhalation challenge studies in Montreal, Canada. The challenges were negative in 29 workers and positive in 26 workers. Isocyanate antibodies were estimated by ELISA index. The mean immunoglobulin-G indices were found to be significantly higher in the challenge-positive workers, and there was a similar trend for the immunoglobulin-E indices. Antibody specificities for **toluene** diisocyanate-human serum albumin, diphenylmethane diisocyanate-human serum albumin, and hexamethylene diisocyanate-human serum albumin were determined by inhibition studies with a variety of isocyanate haptenized carriers. The other isocyanate substituted carriers were either noninhibitory or caused only partial inhibition as contrasted with the complete inhibition achieved by human serum albumin conjugated to the isocyanate to which the worker was exposed. We interpret these specificity studies as indicating that the inhalation of isocyanates results in production of antibody that recognizes new antigenic determinants that develop from the coupling of isocyanates to homologous proteins.
[Grammer LC et al; J Allergy Clin Immunol 86 (1): 94-8 (1990)]**PEER REVIEWED**

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Human Toxicity Excerpts:

Subjects exposed to 0.0010 to 0.0015 ppm of **toluene** diisocyanate demonstrated a normal age and smoking-related rate of decline in forced expiratory volume in 1 second and no evidence that it was related to isocyanate exposures.
[Musk AW et al; J Occup Med 27 (12): 917-20 (1985)]**PEER REVIEWED**

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Probable Routes of Human Exposure:

VAPORS OF THESE COMPD INVARIABLY BECOME AIRBORNE IN POLYMERIZATION REACTIONS, ESP SINCE HEAT & GAS ARE EVOLVED. /**TOLUENE** DIISOCYANATES/ [Hamilton, A., and H. L. Hardy. Industrial Toxicology. 3rd ed. Acton, Mass.: Publishing Sciences Group, Inc., 1974. 335]**PEER REVIEWED**

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Human Toxicity Excerpts:

Two workers who developed asthmatic symptoms were studied with inhalation provocation tests using ... **toluene** diisocyanate. Subjects did not show asthmatic reations to TDI challenge.
[Mapp CE et al; Ann Allergy 54 (5): 424-9 (1985)]**PEER REVIEWED**

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Human Toxicity Excerpts:

Respiratory variables were measured in workers exposed to **toluene** diisocyanate in Canada. Exposure and effect relationships were studied. Results from 95 isocyanate workers were compared with unexposed workers. Exposed workers were grouped according to production areas based on isocyanate concentrations measured. Individual monitors were worn to identify exposure for some workers. Symptoms and history of respiratory illness were compared through questionnaires. Pulmonary function tests included forced vital capacity, forced expiratory volume in 1 second, and forced expiratory flow at 50% and 75% of vital capacity. Pulmonary function was measured at the beginning and end of work shifts on Monday, Wednesday, and Friday of a work week. Regression analysis of exposure concentration and other variables was attempted. When comparisons were adjusted for smoking habits, exposed workers had a significantly lower family history of respiratory complaints. Isocyanate workers had slightly lower base line lung function than comparisons, but had significantly higher declines in pulmonary function over the work week. A 5% or greater decline over a day occurred in 44 percent of exposed but only 22% of comparison workers. Foam line and finishing area workers had greatest declines in forced vital capacity and forced expiratory volume in 1 second. It was concluded that although regression analysis does not show an exposure/effect relationship, an all or none effect may be operating with acute and chronic compartments. However, sample size may have been insufficient. [Holness DL et al; J Occup Med 26 (6): 449-55 (1984)]**PEER REVIEWED**

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Human Toxicity Excerpts:

... The toxicity of inhaled vapors of diisocyanates is summarized. Humans are exposed to high concentrations of diisocyanates in polyurethane industries. Toxic symptoms are acute inflammation with lachrymation, rhinitis, soreness and burning in the throat and upper part of the chest, and coughing. Fire fighters are particularly prone to these clinical symptoms. The toxic limit value for **toluene** diisocyanate is 0.005 ppm. Exposure to diisocyanates can cause asthma.
[Davies RJ; Clinics in Immunology and Allergy 4 (1): 103-23 (1984)]**PEER REVIEWED**

TOLUENE DIISOCYANATE

CASRN: 26471-62-5

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Environmental Water Concentrations:

Toluene diisocyanate has been reported in the waste-water of a furniture manufacturing area in a concn range of 0.1-4.1 mg/l.

[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 299 (1986)]**PEER REVIEWED**

TOLUENE DIISOCYANATE

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Human Toxicity Excerpts:

Toluene diisocyanate may produce a true hemorrhagic syndrome affecting the bone marrow and producing primarily thrombocyte series suppression.
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 303]**PEER REVIEWED**

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Technical grade **toluene** diisocyanate induced chromosome aberrations after a 24 hr treatment in the absence of metabolic activation in human whole blood lymphocyte cultures.
[Maki-Paakkanen J, Norppa H; Toxicol Lett 36 (1): 37-43 (1987)]**PEER REVIEWED**

TOLUENE DIISOCYANATE

CASRN: 26471-62-5

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Environmental Fate:

TERRESTRIAL FATE: Ten days after a spill of 13 tons of **toluene** diisocyanate (TDI) onto swampy, wet forest soil, TDI and toluenediamines were found in the soil(1,2). The TDI solidified and the area was covered with sand. The soil concn of TDI and toluenediamine combined declined from the parts per thousand to parts per million range between 10 days and 12 wk after the spill(2). No TDI was detected in a connecting brook 10 days after the spill(2). After 6 years only TDI-derived polyureas were found at the site(1). In a simulated spill, 5 kg of TDI in a container was covered with 50 kg of sand and 5 kg of water at ambient temperatures and samples taken from the top and bottom of the sand pile. After 24 hr, 5.5% of the TDI remained unreacted and after 8 days 3.5% remained(2). The reaction product was largely polyureas(2).

[(1) IARC Monograph on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. 39: 287-323 (1985) (2) Brochhagen FK, Grieveson BM; Cellular Ploymers 3: 11-7 (1984)]**PEER REVIEWED**

TOLUENE DIISOCYANATE

CASRN: 26471-62-5

For other data, click on the Table of Contents

Human Toxicity Excerpts:

Case reports of keratophathy in polyurethane production workers were examined. The experimental production of similar conditions was studied in cats and a monkey. A male polyurethane worker complained of blurred vision which improved over weekends away from work. The only significant finding on examination of the eyes was subepithelial corneal vesicles of 30 to 50 micrometers in diameter. A second patient, a female worker from the same facility, also complained of attacks of blurred vision. Slit lamp examination showed deep or subepithelial vacuolization only in the palpebral aperture. ... Corneas were normal between 3 day and 2 weeks. Exposure to **toluene** diisocyanate did not result in the clinical appearance of the eye resembling that of the workers.
[Potts AM et al; Am J Indust Med 9 (2): 203-13 (1986)]**PEER REVIEWED**

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Analytic Laboratory Methods:

Matrix: Air. Sample preparation: Draw air through impinger containing aq acid; neutralize; extract (chloroform or **toluene**); react with trifluoroacetic anhydride or heptafluorobutyric anhydride. Procedure: GC/ECD. Limit of detection: 1-5 ug/cu m. /From table/

[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 300 (1986)]**PEER REVIEWED**

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Special Reports:

Toluene diisocyanate; Safety Practitioner 3 (5): 32-3 (1985).

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Special Reports:

DHHS/NTP; Toxicology & Carcinogenesis Studies of Commercial Grade 2,4 (80%)- and 2,6 (20%)-**Toluene** Diisocyanate in F344/N Rats and B6C3F1 Mice(Gavage Studies) Technical Report Series No. 251 (1986) NIH Publication No. 86-2507

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Human Health Effects:

Evidence for Carcinogenicity:

No data are available in humans. Sufficient evidence of carcinogenicity in animals. OVERALL EVALUATION: Group 2B: The agent is possibly carcinogenic to humans.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. S7 72 (1987)]**PEER REVIEWED**

Human Toxicity Excerpts:

TOLUENE DIISOCYANATE (TDI) SENSITIVITY ACCOMPANIED BY NONSPECIFIC BRONCHIAL HYPERRESPONSIVENESS OCCURS IN 5% OF OCCUPATIONALLY EXPOSED WORKERS. THE CASE OF A 32 YR OLD WORKER FOLLOWED LONGITUDINALLY AFTER REMOVAL FROM ISOCYANATE EXPOSURE IS REPORTED. TDI REACTIVITY WAS LOST 11 MONTHS AFTER REMOVAL FROM EXPOSURE & NONSPECIFIC BRONCHIAL HYPERRESPONSIVENESS RESOLVED AFTER 17 MONTHS. IMMUNOPHARMACOLOGIC RESULTS SHOW THAT THE WORKER'S INITIAL DECREASED ABILITY OF LYMPHOCYTES TO PRODUCE CYCLIC-AMP RETURNED TO NEAR NORMAL AFTER 2 YR. IMMUNOGLOBULIN-E ANTIBODIES TO A HUMAN SERUM ALBUMIN TOLYL MONOISOCYANATE CONJUGATE WERE STILL PRESENT THIS TIME.
[BUTCHER BT ET AL; J ALLERGY CLIN IMMUNOL 70 (4): 231 (1982)]**PEER REVIEWED**

ACCIDENTAL SPLASH ... IN EYES OF WORKMEN HAS CAUSED KERATITIS & CONJUNCTIVITIS. ONE CASE ... DESCRIBES "UNUSUAL AMT OF PHOTOPHOBIA & BLEPHAROSPASM" ... SECOND CASE ... INVOLVED SEVERE IRIDOCYCLITIS & SECONDARY GLAUCOMA.
[Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986. 929]**PEER REVIEWED**

WORKERS EXPOSED ... DEVELOPED IRRITATION OF EYES, IRRITATION OR DRYNESS OF THROAT &/OR TIGHTNESS OF CHEST. EXPOSURE TO LEVELS AS LOW AS 0.014 MG/CU M (0.002 PPM) CAN RESULT IN CHRONIC LOSS OF PULMONARY FUNCTION. MORE ACUTE, ASTHMATIC TYPE OF BRONCHITIS IS ... TYPICAL, FRANK ASTHMA MAY OCCUR.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V19 311 (1979)]**PEER REVIEWED**

RESP SYMPTOMS ... IMPROVE ... AFTER REMOVAL FROM /OCCUPATIONAL/ EXPOSURE, BUT ... RE-EXPOSURE TO EVEN MINIMAL CONCN ... PRODUCED RECURRENCE OF ...

SYMPTOMS. HYPERSENSITIVITY ... ARISES AFTER ... INHALATION, & IT HAS BEEN RELATED TO IMMUNOLOGICAL CHANGES ... & TO ALTERED BETA-ADRENERGIC FUNCTION.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V19 311 (1979)]**PEER REVIEWED**

... DOSE-RESPONSE RELATIONSHIP OF ACUTE PULMONARY FUNCTION CHANGES AMONG 112 WORKERS EXPOSED ... TO 0.0035-0.06 MG/CU M (0.0005-0.009 PPM). 2-YR FOLLOW-UP EXAM OF 57 OF WORKERS DISCLOSED DECR IN PULMONARY FUNCTION ... RELATED TO EXPOSURE LEVELS, CONTROLLING FOR AGE, MO EMPLOYED, SMOKING ... & PHYSIQUE.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V19 311 (1979)]**PEER REVIEWED**

A series of workers with exposure to and respiratory symptoms from **toluene** diisocyanate was compared with a group of exposed, asymptomatic workers and with normal controls using immunologic and clinical evaluations. Improved understanding of **toluene** diisocyanate-induced respiratory disease may best be achieved by categorizing the symptomatic workers into at least 3 and possibly 4 groups: immunologic asthma; pre-existing chronic respiratory disease exacerbated or unaffected by **toluene** diisocyanate; asthma coincidental with exposure, and possibly respiratory disease secondary to toxic or inflammatory mechanisms.
[Patterson R et al; Int Arch Allergy Appl Immunol 84 (1): 93-100 (1987)]**PEER REVIEWED**

Subjects exposed to 0.0010 to 0.0015 ppm of **toluene** diisocyanate demonstrated a normal age and smoking-related rate of decline in forced expiratory volume in 1 second and no evidence that it was related to isocyanate exposures.
[Musk AW et al; J Occup Med 27 (12): 917-20 (1985)]**PEER REVIEWED**

Twelve subjects were studied with inhalation challenge testing to **toluene** diisocyanate because of suspected asthma based on a consistent clinical and occupational history. In seven cases, asthma was documented by a positive inhalation challenge to low levels of **toluene** diisocyanate. Six of the seven reactors had persistent respiratory symptoms and required daily treatment even though they had been removed from isocyanate exposure for intervals as long as 12 years (mean 4.5 years). These six reactors had either dual (four cases) or late bronchospasm (two cases) to less than 20 ppb and all had a positive methacholine or cold air challenge prior to study. The one reactor with a negative methacholine challenge had a positive (immediate) bronchospastic response to a challenge performed one week after removal from isocyanate exposure. Five workers had a negative challenge, two of whom had persistent respiratory symptoms and positive methacholine challenges at the time of inhalation testing. ... Respiratory symptoms may persist following long-term removal from occupational exposure to and are associated with nonspecific bronchial hyperreactivity. The sensitivity may also persist for a long time even in the absence of any additional occupational exposure. Long-term prospective studies of symptomatic isocyanate workers are needed to fully define the extent of this problem.

[Moller DR et al; Chest 90 (4): 499 (1986)]**PEER REVIEWED**

Two workers who developed asthmatic symptoms were studied with inhalation provocation tests using ... **toluene** diisocyanate. Subjects did not show asthmatic reations to TDI challenge.
[Mapp CE et al; Ann Allergy 54 (5): 424-9 (1985)]**PEER REVIEWED**

Amine induced asthma was studied in polyurethane foam workers. A total of 12 subjects, occupationally exposed to polyurethane foams, who complained of wheezing and breathlessness at work were tested. Subjects were given 20 to 2000 ug methacholine. Forced expiratory volume in 1 sec was measured. Subjects were challenged with 0.01 ppm **toluene** diisocyanate for 15 min in an atmosphere chamber. Forced expiratory volume in 1 sec was measured. Positive tests were considered as a 15% fall in forced expiratory volume in 1 sec. High sensitivity to methacholine was seen in ten subjects with a 15% fall in forced expiratory volume in 1 sec at <1000 ug; normal subjects responded at 2000 ug. All subjects reacted to **toluene** diisocyanate.
[Cardura F, Moscata G; Brit J Indus Med 41: 552-3 (1984)]**PEER REVIEWED**

... The toxicity of inhaled vapors of diisocyanates is summarized. Humans are exposed to high concentrations of diisocyanates in polyurethane industries. Toxic symptoms are acute inflammation with lachrymation, rhinitis, soreness and burning in the throat and upper part of the chest, and coughing. Fire fighters are particularly prone to these clinical symptoms. The toxic limit value for **toluene** diisocyanate is 0.005 ppm. Exposure to diisocyanates can cause asthma.
[Davies RJ; Clinics in Immunology and Allergy 4 (1): 103-23 (1984)]**PEER REVIEWED**

The respiratory status of factory workers exposed continously to isocyanates over 10 years was studied. A total of 80 workers in two facilities that manufactured fixtures used in the interiors of cars were examined and underwent spirometry before and after work. Of these, 12 were comparisons not exposed to **toluene** diisocyanate. Subjects included those previously examined in 1971. Ventilatory capacity tests were performed inlcuding forced expiratory volume in 1 sec and forced vital capacity testing. Annual decrements were calculated. The mean average concentration of **toluene** diisocyanate was not more than 0.0033 ppm respectively. Subjects who had been studied previously had a mean forced vital capacity of 104.6% and a mean forced expiratory volume in 1 sec of 107% of predicted values. Three subjects with significant obstruction in the lung function tests were smokers. The comparisons in facility 1 had a significantly lower percentage of the predicted forced fital capacity and forced expiratory volume than the exposed population. Most of the data from 1971 for annual decrement calculations were not reliable. A 10% decrement in forced vital capacity and forced expiratory volume in 1 second was indicative of significant postshift decline and would indicate the presence of isocyanate asthma or hypersensitivity; no subject at either facility met the criteria.
[Gee JB; Morgan WKC; J Occup Med 27 (1): 15-8 (1985)]**PEER REVIEWED**

The mechanism by which late asthmatic reactions are induced by **toluene** diisocyanate, a low molecular weight chemical that causes occupational asthma in exposed subjects, is unknown. An investigation was conducted to determine whether early and late asthmatic reactions induced by **toluene** diisocyanate are associated with changes in airway responsiveness to methacholine and airway inflammation as determined by bronchoalveolar lavage. Forced expiratory volume in 1 second was measured before and at regular intervals after exposure to **toluene** diisocyanate and dose-response curves to methacholine and

bronchoalveolar lavage at 8 hr after **toluene** diisocyanate /were performed/ in a group of 6 subjects with late asthmatic reactions and in 6 subjects with only early asthmatic reactions. The same procedure was followed 2 hr after **toluene** diisocyanate in a group of 6 subjects with previously documented late asthmatic reactions and in a group of 6 subjects without any previously documented asthmatic reaction after **toluene** diisocyanate. In subjects with late asthmatic reactions, neutrophils were increased at both 2 hr and 8 hr and eosinophils and airway responsiveness were increased only at 8 hr. By contrast, neutrophils, eosinophils and airway responsiveness were not increased at 8 hr after **toluene** diisocyanate in subjectswith an early asthmatic reaction or at 2 hr after **toluene** diisocyanate in normal control subjects. These results suggest that late asthmatic reactions to **toluene** diisocyanate, and the associated increase in airway responsiveness may be caused by airway inflammation.
[Fabbri LM et al; Am Rev Respir Dis 136 (1): 36-42 (1987)]**PEER REVIEWED**

Technical grade **toluene** diisocyanate induced chromosome aberrations after a 24 hr treatment in the absence of metabolic activation in human whole blood lymphocyte cultures.
[Maki-Paakkanen J, Norppa H; Toxicol Lett 36 (1): 37-43 (1987)]**PEER REVIEWED**

To determine whether late asthmatic reactions and the associated increase in airway induced by **toluene** diisocyanate are linked to airway inflammation, inhibition by prednisone was investigated. Ten "sensitized" subjects were studied in 2 sets of experiments. In the first set, each subject was given no treatment and was studied before and for 8 hr after exposure to **toluene** diisocyanate. In the second set, 2 to 4 wk later, each subject was studied before treatment and then during treatment with prednisone (50 mg once a day for 3 days, orally), both before and after exposure to **toluene** diisocyanate. To assess late asthmatic reactions to **toluene** diisocyanate FEV1 /was measured/ immediately before and after exposure, then hourly for 8 hr. To assess changes in airway responsiveness, a /measurement was made of/ the provocation dose (mg) of methacholine causing a 20% decrease in FEV1 (PD20FEV1) before and 8 hr after exposure to **toluene** diisocyanate. When the subjects received no prednisione treatment, **toluene** diisocyanate caused late asthmatic reactions and increased airway responsiveness. By contrast, when the subjects received prednisone, **toluene** diisocyanate caused no late asthmatic reaction or increased airway responsiveness. Prednisone did not change baseline airway caliber or airway responsiveness. These results suggest that late asthmatic reactions and the associated increase in airway responsiveness induced by **toluene** diisocyanate in "sensitized" subjects may depend on the development of a steroid-responsive acute inflammatory reaction within the airways.
[Fabbri LM; Am Rev Respir Dis 132 (5): 1010-4 (1985)]**PEER REVIEWED**

Case reports of keratophathy in polyurethane production workers were examined. The experimental production of similar conditions was studied in cats and a monkey. A male polyurethane worker complained of blurred vision which improved over weekends away from work. The only significant finding on examination of the eyes was subepithelial corneal vesicles of 30 to 50 micrometers in diameter. A second patient, a female worker from the same facility, also complained of attacks of blurred vision. Slit lamp examination showed deep or subepithelial vacuolization only in the palpebral aperture. ... Corneas were normal between 3 day and 2 weeks. Exposure to **toluene** diisocyanate did not result in the clinical appearance of the eye resembling that of the workers.
[Potts AM et al; Am J Indust Med 9 (2): 203-13 (1986)]**PEER REVIEWED**

Symptoms and lung function of workers exposed to isocyanates in polyurethane foam factories were studied. A group of 67 workers was examined for **toluene**-diisocyanate ... exposure. Measurements were made by samples obtained from subject carried pumps. Interviews were also conducted for information of symptoms involving the nose, eyes, upper airways, and lung. Another group of 56 nonexposed workers was determined by spirometry and nitrogen wash out prior to the work shift. The exposed workers were examined again immediately after work. The variables studied were forced expired vital capacity and forced expired volume in 1 second. ... The highest exposure group was foaming machine workers, with a day mean exposure of 0.023 mg/cu m. Nonsmokers showed an increased frequency of symptoms involving the nose, throat, and dyspnea. Smokers had no significant increase. Smokers of the exposed group reported coughing. Only smokers reported symptoms classified as chronic bronchitis, with frequency independent of exposure. Decreased forced expired vital capacity and forced expired volume were observed in the exposed group. This group also showed increased expired vital capacity. Lung function impairment was restricted to smokers. Spirometric and nitrogen washout variables did not change significantly during the work shift. Decreasing spirometric values with increased exposure was seen in smokers. Conclusions indicate that mean exposure of 0.01 mg/cu m/day to isocyanates may give an increased frequency of symptoms in nonsmokers.
[Alexanderson R et al; Internat Archives of Occup Environ Health 55 (2): 149-57 (1985)]**PEER REVIEWED**

A survey of the incidence of occupational asthma in a steel coating factory was conducted. The survey was prompted by two male employees developing symptoms suggestive of occupational asthma. The cohort consisted of 221 males employed in the coating shop. A respiratory questionnaire was administered. Spirometric tests were conducted. Peak expiratory flow rate studies were performed on 50 subjects. Twenty one subjects reported symptoms of occupational asthma. Sixty three had other work related symptoms and 58 had respiratory symptoms unrelated to work. The mean length of employment of the subjects with asthmatic symptoms was 7.7 years. All symptomatic subjects had significantly reduced 1 second forced expiratory volumes, compared to asymptomatic workers. 21% of the peak expiratory flow rates were indicative of work related asthma. Two symptomatic subjects were administered inhalation challenge tests with **toluene** diisocyanate after it was discovered that one of the coatings that had been used for 8 years released **toluene** diisocyanate during the coating process. Both subjects showed decreases in forced expiratory volumes of at least 15% below the baseline values. Environmental sampling for **toluene** diisocyanate indicated concentrations ranging from below 0.001 to 0.026 ppm. The coating containing **toluene** diisocyanate was removed from the process. A follow-up survey conducted 1 year later showed that 17 of the symptomatic subjects had become asymptomatic or improved.
[Venables KM et al; Brit J Indus Med 42 (8): 517-24 (1985)]**PEER REVIEWED**

The presence of different thresholds on bronchial reactivity to **toluene** diisocyanate was tested in 20 spray painters employed in the furniture industry and affected by TDI induced asthma. Bronchial provocation tests failed to demonstrate nonspecific hyperreactivity to methacholine. Exposure of the workers to **toluene** diisocyanate in concentrations ranging from 0.02 to 0.25 ppm demonstrated the occurrence of low, moderate and high thresholds of airways response to **toluene** diisocyanate in nine, seven and four patients, respectively. There was no association between the **toluene** diisocyanate response threshold and the positive response pattern to the lower range of **toluene** diisocyanate levels, but six of the nine patients with low threshold of response to **toluene** diisocyanate and six of the 11

patients with moderate or high thresholds had nonspecific bronchial hyperreactivity. The response to **toluene** diisocyanate also was not associated with the duration of the asthmatic condition, smoking, cessation of work or nonspecific response to methacholine. The pattern of response was not dose dependent in ten of 13 patients who had two positive bronchial provocation tests with different levels of **toluene** diisocyanate, although dual responses were recorded in three patients who had late reactions at low concentrations of **toluene** diisocyanate. The value of forced expiratory volume in one second, recorded during immediate reactions, showed a dose response relationship, in that it declined by 28.4% at lower **toluene** diisocyanate levels as compared to 38.3% following inhalation of higher doses of the compound; no such association was established for the late reaction to **toluene** diisocyanate. The results conclude that patients who are sensitive to **toluene** diisocyanate may have different thresholds of response to the agent.
[Paggiaro PL et al; Respiration 50 (3): 167-73 (1986)]**PEER REVIEWED**

Respiratory variables were measured in workers exposed to **toluene** diisocyanate in Canada. Exposure and effect relationships were studied. Results from 95 isocyanate workers were compared with unexposed workers. Exposed workers were grouped according to production areas based on isocyanate concentrations measured. Individual monitors were worn to identify exposure for some workers. Symptoms and history of respiratory illness were compared through questionnaires. Pulmonary function tests included forced vital capacity, forced expiratory volume in 1 second, and forced expiratory flow at 50% and 75% of vital capacity. Pulmonary function was measured at the beginning and end of work shifts on Monday, Wednesday, and Friday of a work week. Regression analysis of exposure concentration and other variables was attempted. When comparisons were adjusted for smoking habits, exposed workers had a significantly lower family history of respiratory complaints. Isocyanate workers had slightly lower base line lung function than comparisons, but had significantly higher declines in pulmonary function over the work week. A 5% or greater decline over a day occurred in 44 percent of exposed but only 22% of comparison workers. Foam line and finishing area workers had greatest declines in forced vital capacity and forced expiratory volume in 1 second. It was concluded that although regression analysis does not show an exposure/effect relationship, an all or none effect may be operating with acute and chronic compartments. However, sample size may have been insufficient.
[Holness DL et al; J Occup Med 26 (6): 449-55 (1984)]**PEER REVIEWED**

Toluene diisocyanate may produce a true hemorrhagic syndrome affecting the bone marrow and producing primarily thrombocyte series suppression.
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 303]**PEER REVIEWED**

All workers develop eye, nose, and throat irritation at 0.5 ppm. Sensitized individuals may manifest symptoms at levels as low as 0.02 ppm.
[Ellenhorn, M.J. and D.G. Barceloux. Medical Toxicology - Diagnosis and Treatment of Human Poisoning. New York, NY: Elsevier Science Publishing Co., Inc. 1988. 880]**PEER REVIEWED**

A worker developed **toluene** diisocyanate induced asthma in 1974. On reassessment, 11 yr after leaving the chemical plant where **toluene** diisocyanate was produced, he had no respiratory symptoms and normal bronchial reactivity in response to methacholine, and showed no reaction when challenged with a

subirritant concn of **toluene** diisocyanate. He developed asthma within five months of returning to the workplace. Repeat challenge testing showed bronchial hyperreactivity to methacholine and to the specific sensitising agent, **toluene** diisocyanate. This clinical pattern could be due to underlying **toluene** diisocyanate sensitivity with resolution and reappearance of hyperresponsiveness to methacholine and **toluene** diisocyanate reactivity associated with workplace **toluene** diisocyanate exposure. Alternatively, this worker may have developed sensitisation to **toluene** diisocyanate anew.
[Banks DE, Rando RJ; Thorax 43 (8): 1988 660-2]**PEER REVIEWED**

An investigation of the persistence of isocyanate induced asthma in workers with negligible occupational exposure was carried out. Six asthmatic workers, proven to be **toluene** diisocyanate sensitive by inhalation challenge testing in a longitudinal study of respiratory health risks associated with polyurethane foam production, were examined. The subjects were followed for 5 yr during which they completed a respiratory symptom questionnaire annually. Pulmonary function and responsiveness to methacholine challenge were measured annually. **toluene** diisocyanate concn in their breathing zones were measured. After the original survey the six subjects were transferred to areas thought to have negligible **toluene** diisocyanate exposures. None of the subjects had respiratory or asthmatic complaints before they started work in polyurethane production. The respiratory symptoms of the subjects did not improve during the followup period. All six had bronchial hyperresponsiveness to methacholine that did not resolve over time. Three subjects demonstrated deficits in 1 second forced expiratory volume of greater than 15% on one of the testing days during the followup period. The need for less or additional asthma therapy of the subjects could not be predicted. The mean time weighted average **toluene** diisocyanate exposure experienced by the subjects was 0.64 ppb; less than 5% of the OSHA standard of 20 ppb. It was concluded that although the outcome of isocyanate induced asthma cannot be predicted, the asthmatic symptoms of these workers have persisted despite the negligible **toluene** diisocyanate exposures.
[Banks DE et al; Chest 97 (1): 121-5 (1990)]**PEER REVIEWED**

The prevention of airway inflammation caused by **toluene** diisocyanate by prednisone was studied. Healthy **toluene** diisocyanate sensitive individuals were exposed to 0.018 ppm **toluene** diisocyanate in a test chamber. Bronchoalveolar lavage fluid was collected with a flexible fiberoptic bronchoscope. The lavage fluid was spun in a cytocentrifuge and stained with May/Grunwald/Giemsa for differential cell count. The total cell count was performed on resuspended cell pellets. A late asthmatic response was characterized by the occurrence of less than 20% of free expiratory volume in 1 second. The airway responsiveness was assessed by the reaction to methacholine. The cumulative dose of methacholine that produced a 20% decrease in forced expiratory volume in 1 second was used to measure airway responsiveness. Five subjects who received no prednisone treatment developed a late or dual asthmatic reaction. The albumin concn and total number of cells increased in subjects that were given no prednisone compared to controls. There was a significant increase in the number of neutrophils and a small increase in eosinophilia. There was no significant difference in the counts of other cell types. Results suggest that **toluene** diisocyanate induce late asthmatic reactions causing airway inflammation and that prednisone inhibits these reactions.
[Boschetto P et al; J Allergy Clin Immunol 80 (3):261-267 (1987)]**PEER REVIEWED**

Two men were exposed to **toluene** diisocyanate atmospheres at three different air concn (ca 25, 50 and 70 ug/cu m). The **toluene** diisocyanate atmospheres were generated by a gas-phase permeation method, and the exposures were performed in an 8-cu m stainless-steel test chamber. The effective exposure

period was 4 hr. The isomeric composition of the air in the test chamber was 30% 2,4-**toluene** diisocyanate and 70% 2,6-**toluene** diisocyanate. The concn of **toluene** diisocyanate in air of the test chamber was determined by an HPLC method using the 9-(N-methyl-amino-methyl)-anthracene reagent and by a continuous-monitoring filter-tape instrument. Following the hydrolysis of plasma and urine, the related amines, 2,4-toluenediamine and 2,6-toluenediamine, were determined as pentafluoropropionic anhydride derivatives by capillary gas chromatography using selected ion monitoring in the electron impact mode. In plasma, 2,4- and 2,6-toluenediamine showed a rapid-phase elimination half-time of ca 2-5 hr, and that for the slow phase was greater than 6 days. A connection was observed between concn of 2,4- and 2,6-**toluene** diisocyanate in air and the levels of 2,4- and 2,6-toluenediamine in plasma. The cumulated amount of 2,4-toluenediamine excreted in the urine over 24 hr was ca 15%-19% of the estimated inhaled dose of 2,4-**toluene** diisocyanate, and that of 2,6-toluenediamine was ca 17%-23% of the inhaled dose of 2,6-**toluene** diisocyanate. A connection was found between the cumulated (24 hr) urinary excretion of 2,4- and 2,6-toluenediamine and the air concn of 2,4- and 2,6-**toluene** diisocyanate in the test chamber.
[Brorson T et al; Int Arch Occup Environ Health 63 (4): 253-9 (1991)]**PEER REVIEWED**

Thirty factory workers whose annual exposure to **toluene** diisocyanate amounted to 280 hr were examined. Seven of them had been removed from their jobs for presenting respiratory symptomatology and a further five were removed for presenting bronchial asthma. Their medical histories were consulted and further measures were taken such as a radiological thorax study, total immunoglobulin-E, **toluene** diisocyanate, diphenylmethane diisocyanate and hexamethylene diisocyanate RAST, a basal spirometric study and finally a provocation test. The Rast proved negative in every case. In the spirometric study carried out on the provocation test, four cases showed a significant decrease in the forced expiratory volume in 1 second over 20% and over 40% in the FMEF and PEFR. There was no connection between the four patients who presented an elevated total immunoglobulin-E and the four who presented a positive provocation test. The provocation test proved negative in five of the seven patients removed from their places of work. Two of the four workers who responded positively to the provocation test remained in their places of work during the **toluene** diisocyanate foam test without showing any symptoms. The patients who presented symptoms did not appear to present bronchial obstruction during the provocation test. Nonetheless, patients who seemingly had not shown any symptoms presented what appeared to be bronchial obstruction.
[Duce F et al; Allergol Immunopathol (Madr) 16 (3): 139-44 (1988)]**PEER REVIEWED**

The nature of neurohumoral regulation was studied in 125 healthy workers, aged 20-40 yr, with different length of service and **toluene** diisocyanate exposure levels. Adrenal gland activity and some haematological parameters were determined. Neurohumoral regulation of adaptation processes in **toluene** diisocyanate exposed persons seemed to display some cyclicity, somehow related to the length of service. Two early regulatory phases (service up to 3 yr) had common features unrelated to the exposure levels, while after 3 yr of employment some dissimilarities evolved which did depend on the **toluene** diisocyanate exposure levels.
[Ermakova GA, Kryzanovskaja NA; Gigiena truda i Professional'nye Zabolevanija (7): 22-35 (1988)]**PEER REVIEWED**

Sensitized subjects may develop symptoms of asthma after exposure to isocyanates in their place of work. After challenge with isocyanates in the laboratory, sensitized subjects develop immediate, late and

dual asthmatic reactions. **Toluene** diisocyanate might cause late asthmatic reactions and increase bronchial responsiveness by causing an acute inflammatory reaction in the airways, and that airway inflammation may be responsible for persistence of occupational asthma induced by isocyanates. To test these hypotheses, sensitized subjects were examined during asthmatic reactions induced by exposure to **toluene** diisocyanate in the laboratory. It was observed that late and dual, but not early, asthmatic reactions are associated with a transient increase of bronchial responsiveness which is associated with an acute inflammatory reaction of the airways characterized by an increase of neutrophils followed by eosinophils, by an increase of leukotriene B4 and albumin in bronchoalveolar lavage fluid, and that all these effects are inhibited by steroids. Longitudinal studies suggest that the majority of subjects with occupational asthma continue to have persistent asthma months and yrs after the cessation of exposure, and the results of our studies combined with the results of studies performed by others suggest that the persistence of asthma may be related to the persistence of airway inflammation.
[Fabbri LM et al; Eur Respir J (Suppl 13): 136-38 (1991)]**PEER REVIEWED**

A shortened protocol was developed for the epidemiological measurement of bronchial responsiveness to methacholine without compromising sensitivity, power, precision or safety, and without distorting the numerical value of the PD20.FEV1 (the cumulative dose from a doubling incremental sequence which provokes a 20% decrement in forced expiratory volume in 1 second). It was used in a survey of 254 polyurethane workers (83% of the eligible workforce) exposed occupationally to **toluene** diisocyanate. The mean duration of each test proved to be 38 min, it was well tolerated and 64 workers (25%) proved to be reactors. PD20.FEV1 appeared to be distributed unimodally. It was significantly correlated with questionnaire records of shortness of breath, chest tightness, and wheeze; and with pre-shift forced expiratory volume in 1 second and FEF25-75. Even the reactors requiring the highest dose of 640 cumulative inhalation units (1 unit = one 8.9 ul inhalation of methacholine 1 mg/ml) to generate a PD20 measurement reported significantly more wheeze than the non-reactors. This indicates that the test had clinical meaning throughout its dose range of 0.3-640 units. No correlation was found between PD20 and individual changes in ventilatory function across the working shift, but mean shift changes were negligible and not statistically significant. PD20 was also found to be unrelated to age, sex, race, smoking, cough and atopy.
[Hendrick DJ; Bull Eur Physiopathol Respir 23 (6): 555-9 (1987)]**PEER REVIEWED**

Among the painters handling polyurethane varnish in two furniture manufacturing factories with high **toluene** diisocyanate exposure (0.79 mg/cu m and 0.31 mg/cu m), 26.3% and 15% subjects, respectively displayed asthmatic symptoms, lung function loss, and an increment in mast cell degranulation percentage specific to **toluene** diisocyanate. Some cases of **toluene** diisocyanate linked contact dermatitis were also found among them, being elucidated by positive patch testing to **toluene** diisocyanate. However, the previous abnormalities could not be verified among the painters from another factory with **toluene** diisocyanate concn below the TLV of it (0.11 mg/cu m). It was concluded that both pulmonary hypersensitivity and contact sensitization to **toluene** diisocyanate had occurred in some of the painters included in this study, and that the immunologic effects of **toluene** diisocyanate was concn dependent.
[Huang J et al; Arch Environ Contam Toxicol 21 (4): 607-11 (1991)]**PEER REVIEWED**

The importance of airways inflammation for the development of bronchial hyperresponsiveness and for

exacerbation of asthma was investigated in subjects with occupational asthma. Subjects sensitized to isocyanates, a small molecular weight compound that causes occupational asthma were examined. Studies in asthmatic subjects sensitized to **toluene** diisocyanate demonstrated that late, but not early, asthmatic reactions induced by **toluene** diisocyanate were associated with an acute increase in bronchial responsiveness, and with a marked infiltration of neutrophils and a slight infiltration of eosinophils into the airways, both prevented by steroids. As the late asthmatic reactions and the increase in responsiveness induced by **toluene** diisocyanate were prevented by steroids, but not by indomethacin, it was speculated that cell membrane phospholipid metabolites, which are inhibited by steroids but not by indomethacin, may be involved in **toluene** diisocyanate induced hyperresponsiveness. The results of these studies suggest that bronchial hyperresponsiveness and exacerbation of asthma may be related to inflammation of the airways and that cell membrane phospholipid metabolites may be involved.
[Mapp CE et al; Bull Eur Physiopathol Respir 23 (6): 583-6 (1987)]**PEER REVIEWED**

A study of individuals with occupational asthma induced by **toluene** diisocyanate was conducted. This was a followup of 35 patients, 25 males, with a history of isocyanate sensitization. They had 3 to 41 years' occupational exposure to isocyanate compounds. The subjects had been diagnosed with isocyanate asthma on the basis of their response to bronchial challenge with **toluene** diisocyanate. They were examined an average of 11 mo after diagnosis. They underwent bronchial challenge with **toluene** diisocyanate and methacholine. Forced expiratory volumes in 1 second were measured. Symptoms reported by the subjects were recorded. Twenty seven subjects were still asthmatic at followup as shown by a positive reaction to **toluene** diisocyanate challenge. They showed a deterioration in their forced expiratory volumes in 1 second and response to methacholine similar to that seen at diagnosis. Seventy seven percent of these subjects continued to have recurring attacks of dyspnea, wheezing, and cough which required medication. Twenty two of the asthma subjects had been removed from exposure. Subjects who recovered (did not react to **toluene** diisocyanate at the followup examination) showed an improvement in their forced expiratory volumes in 1 second and a reduced response to methacholine. At the time of diagnosis they tended to have an immediate or dual asthmatic reaction and were younger than the other subjects. The asthmatic subjects had dual or late reactions at diagnosis. It was concluded that respiratory symptoms, isocyanate sensitization, and airway hyperresponsiveness may persist for some time after exposure to **toluene** diisocyanate has ended.
[Mapp CE et al; Am Rev Respir Dis 137 (6): 1326-9 (1988)]**PEER REVIEWED**

Six workers with occupational asthma due to **toluene** diisocyanate were studied. For each worker a detailed clinical and occupational history was taken, and lung function measurement and skin intradermal tests for common allergens were carried out. Methacholine inhalation challenge was performed before **toluene** diisocyanate inhalation, and 8 hr after **toluene** diisocyanate inhalation. Methacholine challenge was within normal limits when performed before **toluene** diisocyanate inhalation, but went into the asthmatic range after **toluene** diisocyanate inhalation. These cases provid evidence that asthma can be induced by **toluene** diisocyanate in the absence of airway hyperresponsiveness. They further demonstrate that an isolated negative methacholine inhalation test cannot be used to exclude sensitization to **toluene** diisocyanate. Screening and follow-up studies on workers exposed on **toluene** diisocyanate require serial measurements of airway responsiveness and of variable air-flow obstruction.
[Mapp CE et al; Eur J Respir Dis 68 (2): 89-95 (1986)]**PEER REVIEWED**

The clinical findings and the results of inhalation challenge with **toluene** diisocyanate and methacholine in 113 subjects with a history of exposure to **toluene** diisocyanate and work-related respiratory symptoms are reported. Only some of the subjects (40.7%) had isocyanate asthma, diagnosed by a positive **toluene** diisocyanate inhalation challenge. Most reactors had a dual (30.4%) or a late (41.3%) response. The interval between the last occupational exposure and the specific challenge was significantly shorter in reactors, and among this group the number of immediate reactions to **toluene** diisocyanate decr progressively with an incr interval. The reactors had a significantly higher proportion of positive responses to methacholine and a significantly lower mean PD[1][5] FEV[1] (provocative dose of methacholine which provoked a 15% decrease in forced expiratory volume in 1 second): reactors 557:g, SEM 92.3; non-reactors 1346:g, SEM 128, P < .01. Methacholine challenge could not identify subjects with isocyanate asthma.
[Moscato G et al; J Occup Med 33 (6): 720-5 (1991)]**PEER REVIEWED**

Toluene diisocyanate is commonly used as the 2,4 and 2,6 isomers. NIOSH has estimated that 50,000 to 100,000 workers in the United States are regularly exposed to diisocyanates. As of 1977, 49,996 were estimated to be exposed to **toluene** diisocyanate alone. Methods for measuring diisocyanate exposures were considered. The current American Conference of Governmental Industrial Hygienists' recommended standard is 0.005 ppm time weighted average and 0.02 ppm peak for four 15 min periods a day. Results of exposure measurements taken in industry were summarized. Health effects of diisocyanates were discussed. In laboratory animals, **toluene** diisocyanate has caused inflammation and necrosis when applied directly to the skin, conjunctivitis when applied to the eyes, and rhinitis, laryngitis, tracheitis, bronchitis, and pneumonia when inhaled. Diisocyanates are potent pulmonary sensitizers capable of causing isocyanate asthma in humans. They can induce nonspecific airways disease and hypersensitivity pneumonitis after either acute or chronic exposure.
[Musk AW et al; Am J Ind Med 13 (3): 331-49 (1988)]**PEER REVIEWED**

A 46 yr old man who had worked in a paint processing plast for over 29 yr was admitted to our hospital with complaints of nocturnal dyspnea and dry cough. A chest X-ray film showed diffuse granular shadows in bilateral lungs. Pulmonary function tests revealed reduction of diffusing capacity and restrictive impairments. Hypersensitivity pneumonitis due to isocyanates was speculated from his occupational history and clinical course. Positive skin tests against **toluene** diisocyanate-human serum albumin and diphenylmethane diisocyanate-human serum albumin, precipitating antibody against **toluene** diisocyanate-human serum albumin, and negative lymphocyte stimulating tests of peripheral blood and bronchoalveolar lavage fluid were also noticed. Environmental provocation test was positive. Histological findings of transbronchial lung biopsy specimens showed diffuse alveolitis and Masson body, but no granulomas. According to these results, the patient was diagnosed as hypersensitivity pneumonitis due to **toluene** diisocyanate. Type III allergy of Gell-Coombs seems to participate in this case. The granulomatous lesion is seen less frequently in isocyanate related hypersensitivity pneumonitis than in hypersensitivity pneumonitis induced by organic dusts, which suggests the difference in immunological and histological reactions between both types of hypersensitivity pneumonitis.
[Nozawa S et al; Nippon Kyobu Shikkan Gakkai Zasshi 27 (11): 1335-41 (1989)]**PEER REVIEWED**

Pulmonary function tests were done and compared to current and past potential exposure levels of **toluene** diisocyanate for 57 **toluene** diisocyanate manufacturing workers and 89 workers not exposed to **toluene** diisocyanate or other known respiratory hazards. The average **toluene** diisocyanate plant experience was 4.1 yr (standard deviation = 2.8). Routine industrial hygiene measurements have shown

toluene diisocyanate exposure below a time-weighted average of 0.005 ppm and a short-term exposure level of 0.02 ppm. A certified industrial hygienist ranked department and job classification by level of potential exposure to **toluene** diisocyanate (none, low, moderate, and high). A questionnaire was administered to determine the prevalence of respiratory symptoms and smoking habits. Using backward regression analysis, cumulative pack-years of cigarette smoking and prevalence of lower respiratory symptoms were statistically significant predictors of a standardized forced expiratory volume at 1 second; however, **toluene** diisocyanate exposure, whether classified as current, highest career level, cumulative, or cumulative highest-to-date, was not associated with a decline in forced expiratory volume.
[Olsen GW et al; J Occup Med 31 (8): 664-7 (1989)]**PEER REVIEWED**

Fifty seven polyurethane foam manufacturing workers and 24 reference workers were followed for 4 yr to clarify the effects on pulmonary function of working in polyurethane foam factories with exposure to **toluene** diisocyanate. No significant differences in the average annual losses of pulmonary function for 4 yr were observed among the 28 polyurethane foam workers whose **toluene** diisocyanate exposure levels were very low (mean = 0.1 ppb, group L), the remaining 29 polyurethane foam workers with mean **toluene** diisocyanate exposure of 5.7 ppb (group H), and the reference workers. However, 15 polyurethane foam workers in group H who had experienced peak exposure excursions to 30 ppb or above with a mean concn of 8.2 ppb showed significantly larger average annual losses in percentage maximal mid-expiratory flow, forced expiratory volume in 1 sec ratio to vital capacity, and forced expiratory flow at 25% of forced vital capacity than expected, and significantly larger average annual losses in some obstructive pulmonary function indices than those of the 14 remaining polyurethane foam workers in group H whose peak exposure excursion levels were 3-14 ppb with a mean time-weighted average of 1.7 ppb, group L, and the reference workers. These findings suggest that the peak exposure excursion level of **toluene** diisocyanate might be important in inducing obstructive pulmonary function changes in the polyurethane foam workers rather than the TWA exposure levels, though further comparative studies of the AAL in those who are exposed to different peak exposure excursion levels but the same mean exposure levels are necessary. From the standpoint of prevention, the proposition that peak exposure excursion levels exceeding 20 ppb should be avoided is reasonable.
[Omae K et al; Int Arch Occup Environ Health 63 (8): 565-9 (1992)]**PEER REVIEWED**

To evaluate the morphologic basis of the different outcomes of **toluene** diisocyanate asthma after quitting occupational exposure, ten patients with **toluene** diisocyanate asthma were examined who showed, at diagnosis, a positive **toluene** diisocyanate challenge test and nonspecific bronchial hyperresponsiveness to methacholine. After diagnosis, all patients ceased work and a 4 to 40 mo follow-up was obtained with three to eight determinations of the cumulative dose producing a 15% fall in forced expiratory volume in 1 second to methacholine in each patient. Bronchoalveolar lavage and biopsy of bronchial muscosa were performed 3 to 39 mo after cessation of work, in the absence of acute exacerbations of the disease. Total cell count in bronchoalveolar lavage fluid was moderately increased in four of ten patients, eosinophils were increased in five of ten patients, and neutrophils were increased in eight of ten patients. Mucosal biopsy specimens of main or lobar bronchi were available in eight of ten patients; epithelial damage and thickening of basement membrane was observed in almost all patients, as well as a mild to moderate inflammatory reaction in the submucosa, mainly represented by lymphocytes, eosinophils, and neutrophils. No relationship was observed between the cellularity of bronchoalveolar lavage and the degree of nonspecific bronchial hyperresponsiveness at the time of bronchoalveolar lavage; mean values of total cells and differential count were not different between patients with

presence or absence of the different histologic findings. Mucosal biopsy and bronchoalveolar lavage were performed also in four subjects exposed to dusts without respiratory symptoms or nonspecific bronchial hyperresponsiveness; similar findings were obtained except for the absence of eosinophils in bronchoalveolar lavage and a lesser degree of basement membrane thickening and inflammatory reaction in the submucosa. The study of the changes in nonspecific bronchial hyperresponsiveness after quitting exposure showed that five of ten patients had a significant improvement in nonspecific bronchial hyperresponsiveness to methacholine, as evaluated by a positive significant linear regression between months of work cessation and forced expiratory volume in 1 sec of methacholine; only one of these five patients had an increased number of eosinophils in bronchoalveolar lavage fluid. By contrast, four of the five patients with persistent nonspecific bronchial hyperresponsiveness after quitting exposure had an increased number of eosinophil in bronchoalveolar lavage. It is suggested that persistent nonspecific bronchial hyperresponsiveness in **toluene** diisocyanate asthma after cessation of work may be related to an inflammatory reaction in which eosinophil infiltration seems to be a major determinant.
[Paggiaro P et al; Chest 98 (3): 536-42 (1990)]**PEER REVIEWED**

The effect of cessation of exposure to **toluene** diisocyanate was studied in six patients with **toluene** diisocyanate induced asthma, proved by a positive inhalation challenge with **toluene** diisocyanate. Bronchial challenges with **toluene** diisocyanate and methacholine were performed, and lobar bronchial biopsies were taken at diagnosis and 6 mo later, after cessation of exposure. Biopsies from four nonasthmatic control subjects were also examined. At diagnosis, asthmatic subjects had thickened reticular basement membrane ($p < 0.05$) and increased numbers of mononuclear cells ($p < 0.05$) and eosinophils ($p < 0.05$) in the lamina propria when compared with control subjects. Electron microscopy showed degranulation of eosinophils and mast cells in asthmatics. Six months after cessation of exposure, the thickness of reticular basement membrane was significantly reduced compared with that at diagnosis ($p < 0.05$), and it decr to values similar to those of control biopsies. Inflammatory cell numbers in bronchial mucosa of asthmatic subjects did not change significantly 6 mo after removal from exposure, and degranulation of eosinophils and mast cells was still present. At the end of the study, airwa hyperresponsiveness to methacholine and/or sensitivity to **toluene** diisocyanate persisted in most of the asthmatic patients despite the cessation of exposure and the disappearance of asthmatic symptoms. In conclusion, in patients with occupational asthma induced by **toluene** diisocyanate, the avoidance of exposure to the sensitizing agent for 6 mo is able to reverse the reticular basement membrane thickening in the bronchial mucosa, but th inflammatory cell infiltrate, the specific sensitivity to **toluene** diisocyanate, and the nonspecific airway hyperreactivity may persist.
[Saetta M et al; Am Rev Respir Dis 145 (1): 169-74 (1992)]**PEER REVIEWED**

Forty-three workers exposed to low levels of **toluene** diisocyanate during the process of producing polyurethane forms were examined immunologically for immunoglobulin-G, A, M, and E and serum enzyme activities such as serum angiotensin converting enzyme, serum lysozyme and glycylproline dipeptidyl aminopeptidase. Air concn of **toluene** diisocyanate was annually measured in various places of work during the past five years from 1979 to 1983. The results obtained in the present study were as follows. The air concn of **toluene** diisocyanate at all places of work was below the permissible concn level of 0.02 ppm throughout the study period. Subjective symptoms and abnormal findings on chest X-ray considered directly related to **toluene** diisocyanate exposure were no observed. No remarkable abnormal findings in blood cell counts and in serum biochemical studies could be seen in any of the workers. The serum immunoglobulin-G levels in workers directly exposed to **toluene** diisocyanate were

significantly higher ($p < 0.05$) than those in workers indirectly exposed to **toluene** diisocyanate and in non-exposed workers. In the study of serum enzymatic activity, serum lysozyme activity in workers exposed directly to **toluene** diisocyanate was significantly higher ($p < 0.01$) than those in workers indirectly exposed to **toluene** diisocyanate and in non-exposed workers.
[Taniwaki H et al; Sangyo Igaku 29 (2): 130-5 (1987)]**PEER REVIEWED**

A case of building related health complaints was investigated with respect to the relationship among frequency of symptoms, antibodies to albumin conjugates of formaldehyde, **toluene** diisocyanate, and trimellitic anhydride, and volatile organic chemicals. The indoor air concn of volatile organic chemicals, formaldehyde, **toluene** diisocyanate and trimellitic anhydride did not exceed Fed-OSHA and ACGIH permissible standards. However, formaldehyde concn ranged between 0.05 and 0.08 ppm. The reported symptoms were multiple, involving the eyes, nose, sinuses, throat, lungs, skeletomuscular system and central nervous system. Anti-formaldehyde, **toluene** diisocyanate, and trimellitic anhydride isotypes were found in 12 of 14 full-time employees and were nondetectable in one part-time employee. The data suggest that a synergistic immunological response to airborne chemicals may be occurring in these subjects. In conclusion, immunological monitoring of affected individuals where chemicals are suspected may prove to be useful in future investigations of building related illness.
[Thrasher JD et al; Am J Ind Med 15 (2): 187-95 (1989)]**PEER REVIEWED**

Diisocyanate inhalation tests (maximal concn, 20 ppb; exposure time, 1-2 hr) were performed using **toluene** diisocyanate (TDI, n = 15) and diphenylmethane diisocyanate (MDI, n = 7) as well as methacholine challenges in 19 workers who had a clinical history of **toluene** diisocyanate/diphenylmethane diisocyanate induced asthma. Additionally volunteers were tested who had n previous contact with diisocyanates: 10 healthy individuals with a negative methacholine test and 14 patients with asthma and a positive methacholine test were exposed to **toluene** diisocyanate. In all, 1 of the normal volunteers and 3 of the patients with asthma unrelated to diisocyanates showed a positive airway reaction to **toluene** diisocyanate, and 13 of the 19 diisocyanate workers displayed a positive result in the **toluene** diisocyanate/diphenylmethane diisocyanate inhalation test; however, only 6 of these 13 individuals reacted to methacholine. Furthermore, 3 of the 6 patients with a negative **toluene** diisocyanate/diphenylmethane diisocyanate challenge test demonstrated a significant response to methacholine. It was concluded that bronchial hyperreactivity as evaluated by the methacholine challenge test is not closely related to isocyanate induced bronchoconstriction and, therefore, the metacholine challenge is only of limited diagnostic value in patients with suspected isocyanate induced asthma.
[Vogelmeier C et al; Int Arch Occup Environ Health 63 (1): 9-13 (1991)]**PEER REVIEWED**

An outbreak of occupational asthma due to **toluene** diisocyanate among industrial workers was described. Four employees at a velcro/like tape manufacturing factory in Taipei, Taiwan were seen in an outpatient clinic complaining of cough, shortness of breath, and wheezing. The symptoms became worse at night and improved after long holidays. The patients' job involved applying an adhesive to the tape. Thirty eight of 45 employees were interviewed by questionnaire and given pulmonary function tests. The pulmonary function tests were given during a workday, after a 10 day holiday, and 5 mo after control measures such as process isolation, improved ventilation, and substitution for **toluene** diisocyanate were instituted. Industrial hygiene sampling for **toluene** diisocyanate was conducted. Fourteen workers had symptoms of asthma or asthmatic bronchitis. The highest attack rate occurred in workers employed in the

tape processing area where the adhesive was applied. Workers in the tape processing area also showed the greatest decr in 1 second forced expiratory volume and forced vital capacity over the workday. Mean **toluene** diisocyanate concn ranged from 0.012 to 0.047 ppm, the highest occurring in the tape processing area and the lowest in the weaving area. The prevalence of asthmatic symptoms was significantly correlated with **toluene** diisocyanate concn. The forced expiratory volume in 1 second and forced vital capacity values were significantly improved after the 10 day holiday and 5 mo after the control methods were instituted. No asthmatic symptoms were reported after 5 mo. It was concluded that **toluene** diisocyanate was responsible for the outbreak and improving the work environment was effective in reducing exposure to **toluene** diisocyanate.
[Wang JD et al; Am J Ind Med 14 (1): 73-8 (1988)]**PEER REVIEWED**

A 41 yr old automobile paint sprayer showed the clinical features of hypersensitivity pneumonitis 1 wk after he had begun to work with paint materials containing **toluene** diisocyanate. His symptoms began 6 to 8 hr after exposure to the agent and spontaneously disappeared by the next morning. He had diffuse, fine reticulonodular shadows on a chest roentgenogram and a restrictive impairment of pulmonary function. Immunoglobulin G antibody to **toluene** diisocyanate-human serum albumin was present in bronchoalveolar lavage fluid and sera: IgA antibody was present only in bronchoalveolar lavage fluid. Also, the patient had sensitized bronchoalveolar lymphocytes to **toluene** diisocyanate-human serum albumin. The histologic findings suggested hypersensitivity pneumonitis. The results of bronchoalveolar lavage, which was repeated on four separate occasions, showed lymphocytosis and a predominance of suppressor cytotoxic T cells. The findings from serial determinations of humoral antibodies showed no changes consistent with the results of clinical and laboratory studies. In contrast, blastogenic responses of bronchoalveolar lymphocytes to **toluene** diisocyanate markedly decr, and the patient showed clinical improvement despite continued exposure to the agent.
[Yoshizawa Y et al; Ann Intern Med 110 (1): 31-4 (1989)]**PEER REVIEWED**

Skin, Eye and Respiratory Irritations:

AS A VAPOR ... /**TOLUENE** DIISOCYANATE/ IS A POWERFUL IRRITANT TO EYES, SKIN, RESPIRATORY TRACT.
[Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984.,p. II-414]**PEER REVIEWED**

Medical Surveillance:

A SCREENING PROGRAM WAS UNDERTAKEN AT A RESEARCH & DEVELOPMENT FACILITY OF A LARGE **TOLUENE**-DIISOCYANATE (TDI) MANUFACTURING CORPORATION. THE PURPOSE WAS TO DETERMINE THE OCCURRENCE OF ANTIBODIES TO TDI IN SELECTED WORKER POPULATIONS. NO TOLYL-REACTIVE IMMUNOGLOBULIN-E ANTIBODIES WERE DETECTED IN SERA WHEN WORKERS WERE EXPOSED ONLY TO AMBIENT TDI CONCN. WORKERS HAD ACUTE EXPOSURES TO TDI AS A RESULT OF SPILLS OR SPLASHES. ANTIBODY RESPONSES DEVELOPED IN 3 OF 4 INDIVIDUALS WHOSE ACUTE EXPOSURES WERE ACCOMPANIED BY IMMEDIATE RESPIRATORY SYMPTOMATOLOGY & A DECREASED FORCED EXPIRATORY VOLUME. AN ANTIBODY RESPONSE DEVELOPED IN 1 OF 9 WORKERS & IMMEDIATE RESPIRATORY

SYMPTOMS, BUT NO SPIROMETRIC CHANGES UPON ACUTE TDI EXPOSURE. ROUTINE SEROLOGIC SCREENING OF WORKERS FOR TOLYL-REACTIVE ANTIBODIES MAY BE OF VALUE IN CONFIRMING SUSPECTED ISOCYANATE EXPOSURE & IN PROVIDING AN EARLY WARNING OF DEVELOPING TDI HYPERSENSITIVITY.
[KAROL MH; J OCCUP MED 23 (11): 741 (1981)]**PEER REVIEWED**

MEDICAL EVALUATIONS OF 15 WORKERS WERE MADE TO DETERMINE THE HEALTH EFFECTS OF EXPOSURE TO TDI, PHOSGENE & TDA. THE FOLLOWING STEPS WERE RECOMMENDED: THE ENTIRE FACTORY POPULATION SHOULD BE SURVEYED PERIODICALLY FOR SYMPTOMS OF LOWER RESPIRATORY TRACT DISEASES & LUNG FUNCTION ABNORMALITIES THAT MAY BE CAUSED BY CHEMICAL EXPOSURE; TDI EXPOSURE SHOULD BE ENDED FOR SENSITIZED WORKERS OR FOR THOSE WITH EXCESSIVE DECLINE IN LUNG FUNCTION.
[COSTELLO RJ, PETERS JM; HEALTH HAZARD EVALUATION DETERMINATION REPORT NO HE-78-31-623, OLIN CORPORATION, ASHTABULA, OHIO 44004; REPORT NIOSH-HE-78-31-623, ORDER NO PB80-195274 (1979)]**PEER REVIEWED**

/Protect/ from exposure those individuals with diseases of blood and liver. Physical exam of exposed personnel annually, incl blood count and liver functions. /**Toluene**-2,4-diisocyanate/
[ITII. Toxic and Hazardous Industrial Chemicals Safety Manual. Tokyo, Japan: The International Technical Information Institute, 1988. 528]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": Whenever medical surveillance is indicated, in particular when exposure to a carcinogen has occurred, ad hoc decisions should be taken concerning ... /cytogenetic and/or other/ tests that might become useful or mandatory. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 23]**PEER REVIEWED**

Comprehensive preplacement medical examinations should be given to each employee. The examination should include a pulmonary function test including FEV1, FVC, and FEV1/FVC, a history of diisocyanate exposure, smoking history, and history of respiratory conditions. The medical data obtained in the pre-placement examination can be used as a base line for periodic examination. Periodic examinations may be useful in detecting a reduction in lung function. Lung function tests, pulmonary history, and pulmonary physical exam should be repeated at least annually. All medical records, including pulmonary function and related medical tests, should be maintained for 30 years.
[Zenz, C. Occupational Medicine-Principles and Practical Applications. 2nd ed. St. Louis, MO: Mosby-Yearbook, Inc, 1988. 1019]**PEER REVIEWED**

Probable Routes of Human Exposure:

Exposure to **toluene** diisocyanate is primarily occupational via inhalation or dermal contact with the aerosol or vapor. Workers may also be exposed through skin contact with freshly cured foam or as a result of spills or splashes. (SRC)

PEER REVIEWED

THE RESPIRATORY HEALTH OF 277 WORKERS IN A NEW **TOLUENE** DIISOCYANATE (TDI) MANUFACTURING PLANT WAS STUDIED PROSPECTIVELY DURING 5 YR OF EXPOSURE. PERSONAL TDI MONITORS WERE USED TO CONTINUOUSLY MEASURE PEAK & 8-HR TIME-WEIGHTED AVG (TWA) CONCN IN MORE THAN 2000 SAMPLES. REGRESSION OF ANNUAL CHANGE ON SMOKING (PACK-YEARS), ATOPIC STATUS & CUMULATIVE TDI EXPOSURE, DICHOTOMIZED AT 68.2 PPB MONTHS INTO LOW & HIGH EXPOSURE GROUPS, SHOWED SIGNIFICANT EFFECTS OF SMOKING ON SPIROMETRIC TESTS & LUNG VOLUMES. AFTER ADJUSTING FOR PACK-YEARS OF SMOKING, THE 74 MEN IN THE HIGH CUMULATIVE TDI EXPOSURE CATEGORY HAD SIGNIFICANTLY LARGER DECLINE IN FEV1 (1-S FORCED EXPIRATORY VOLUME), % FEV (% FORCED EXPIRATORY VOLUME) & FEF25-75% (FORCED EXPIRATORY FRACTION FROM 25 TO 75% VITAL CAPACITY) THAN DID THE 149 MEN IN THE LOW CATEGORY. ANNUAL CHANGE IN FEV1 WAS THEN EXAMINED IN 6 SMOKING-EXPOSURE CATEGORIES: IN NEVER-SMOKERS, AVG ANNUAL DECLINE WAS 38 ML/YR GREATER IN THOSE WITH HIGHER CUMULATIVE TDI EXPOSURE.
[DIEM JE ET AL; AM REV RESPIR DIS 126 (3): 420 (1982)]**PEER REVIEWED**

VAPORS OF THESE COMPD INVARIABLY BECOME AIRBORNE IN POLYMERIZATION REACTIONS, ESP SINCE HEAT & GAS ARE EVOLVED. /**TOLUENE** DIISOCYANATES/
[Hamilton, A., and H. L. Hardy. Industrial Toxicology. 3rd ed. Acton, Mass.: Publishing Sciences Group, Inc., 1974. 335]**PEER REVIEWED**

NIOSH (NOHS Survey 1972-1974) has statistically estimated that 29,284 workers are exposed to TDI in the USA(1). NIOSH (NOES Survey 1981-1983) has statistically estimated that 6,044 workers are exposed to TDI in the USA(2). Since the NOES survey excludes exposure to trade name chemicals which may contain the chemical, occupational exposure could be considerably higher(SRC).
[(1) NIOSH; National Occupational Health Survey (1974) (2) NIOSH; National Occupational Exposure Survey (1983)]**PEER REVIEWED**

Concentration medians for 2,4-**toluene** diisocyanate in 2 plants producing flexible polyurethane foam were 0.70 and 0.33 ppb for the mixing and finishing ends, respectively(1). The respective median values for 2,6-TDI were 0.91 and 1.1 ppb. Maximum concentrations of 2,6-TDI exceeded 64 ppb at the finishing end(1).
[(1) Rando RJ et al; Am Ind Hyg Assoc J 45: 199-203 (1984)]**PEER REVIEWED**

In a Finnish study, TDI vapor concentrations ranged from 25-80 ug/cu m for pouring, 14-44 ug/cu m for paper stripping, and 1-8 ug/cu m for cutting(1). Personal monitors measured 9-34 ug/cu m and 5-30 ug/cu m of the 2,4-isomer for pouring and paper stripping, respectively(1). While 2,4-**toluene** diisocyanate constitutes 80% of TDI, and 2,6-**toluene** diisocyanate 20%, the 2,4-isomer is more reactive so that the concentration of the 2,6-isomer is higher in workplace air(1). The percentage of 2,4-**toluene** diisocyanate to total **toluene** diisocyanate measured with the personal monitors ranged from 29 to 69%(1). TDI levels of 1.3-2.8 ppb were detected in air inside a Swedish factory manufacturing polyurethanes(2).

[(1) Rosenberg C, Savolainen H; J Chromatography 367: 385-92 (1986) (2) Audunsson G et al; Intern J Environ Anal Chem 20: 85-100 (1985)]**PEER REVIEWED**

Mean concn ranges of TDI reported in ambient workplace air were 0.7-710 ug/cu m in TDI production, ND - 1490 ug/cu m during polyurethane foam production, 70-140 mg/cu m during elastomer production, 13 - 1050 ug/cu m during polyurethane foam use, 10-710 ug/cu m during polyurethane spray paint use, and <1-740 ug/cu m during the production of polyurethane-coated wire(1). Mean concn in personal samples ranged from ND-540 ug/cu m during polyurethane foam production and 2-1220 ug/cu m during polyurethane spray foam use(1). Additionally, mean concn of TDI released from insulation in a ship's hold was reported to be 120-150 ug/cu m and that released from coated fabric in a workplace 2-10 ug/cu m(1). During the outdoor application of TDI foam to a 40 ft diameter storage tanks, the mean atmospheric TDI concentration downwind from the spray gun was 0.3 ppm at 8 ft, 0.02 ppm at 40 ft, and 0.002 ppm at 150 ft(2). TDI was not detected more than 8 ft upwind of the spray gun(2). Air samples taken within two ft of the foam surface immediately after spraying had ceased was found to be 0.03 ppm(2). Mean TDI concentrations near the pumping equipment during material transfer was 0.02 ppm(2).
[(1) IARC Monograph on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. 39: 287-323 (1985) (2) Peterson JE et al; Amer Id Hyg Assoc J 23: 345-52 (1962)]**PEER REVIEWED**

Emergency Medical Treatment:

Emergency Medical Treatment:

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The following Overview, *** **TOLUENE** DIISOCYANATE ***, is relevant for this HSDB record chemical.

Life Support:

- This overview assumes that basic life support measures have been instituted.

Clinical Effects:

SUMMARY OF EXPOSURE

0.2.1.1 ACUTE EXPOSURE

- **Toluene** diisocyanate is an irritant to skin, lungs, conjunctiva and gastrointestinal tract. Euphoria, ataxia, mental aberrations, sensitization (primarily respiratory), bronchitis, emphysema and cor pulmonale can occur.

HEENT

0.2.4.1 ACUTE EXPOSURE

- Severe conjunctival irritation and lacrimation from liquid or high vapor concentrations is likely. Lower concentrations may produce a burning or prickling sensation.
- Glaucoma and iridocyclitis have been reported with a splash accident.

RESPIRATORY

0.2.6.1 ACUTE EXPOSURE

- Burning or irritation of the nose and throat, cough, laryngitis, chest pain, and asthmatic syndrome (chemical bronchitis with severe bronchospasm), sensation of oppression or constriction of the chest, bronchitis, emphysema and cor pulmonale may occur.
- Respiratory symptoms may recur several years after discontinuation of exposure.

NEUROLOGIC

0.2.7.1 ACUTE EXPOSURE

- Acute exposures may produce headache, insomnia, euphoria, ataxia, anxiety neurosis with depression, or paranoid tendencies.

GASTROINTESTINAL

0.2.8.1 ACUTE EXPOSURE

- Inhalation of vapor or aerosol may produce vomiting and abdominal pain. Epigastric and substernal pain may be secondary to the paroxysmal or persistent cough associated with inhalation.

DERMATOLOGIC

0.2.14.1 ACUTE EXPOSURE

- Irritation and inflammation are common. Dermal absorption is low.

IMMUNOLOGIC

0.2.19.1 ACUTE EXPOSURE

- Elevated specific IgE and IgG antibodies have been detected in sensitized and exposed workers. The presence of antibodies does is an indicator of exposure

but not of sensitization.

CARCINOGENICITY

0.2.21.1 IARC CATEGORY

- **Toluene** diisocynate has been classified as a 2B agent: possibly carcinogenic to humans, based on sufficient evidence of carcinogenicity in experimental animals and no human data (IARC, 1987).

0.2.21.2 HUMAN OVERVIEW

- **Toluene** diisocyanate is considered a suspected or possible human carcinogen, based on sufficient evidence of carcinogenicity or tumors (spleen, subcutaneous, hepatic, ovarian, peritoneum, mammary gland tissues) in experimental animals (IARC, 1987; US DHHS, 1994; ACGIH, 1995).

Laboratory:

- Monitor respiratory function closely.

Treatment Overview:

ORAL EXPOSURE

- Due to the irritant nature of this substance, emesis is not advised.
- DILUTION: Immediately dilute with 4 to 8 ounces (120 to 240 mL) of milk or water (not to exceed 15 mL/kg in a child).
- ACTIVATED CHARCOAL: Administer charcoal as slurry (240 mL water/30 g charcoal). Usual dose: 25 to 100 g in adults/adolescents, 25 to 50 g in children (1 to 12 years), and 1 g/kg in infants less than 1 year old.
- Monitor patient for respiratory distress. If a cough or difficulty in breathing develops, evaluate for respiratory tract irritation, bronchitis and pneumonia.
- Allergic reaction: Sensitized individuals should be cautioned to avoid further exposure as serious allergic reactions may result.

INHALATION EXPOSURE

- DECONTAMINATION: Move patient to fresh air. Monitor for respiratory distress. If cough or difficulty in breathing develops, evaluate for respiratory tract irritation, bronchitis, or pneumonitis. Administer 100 percent humidified supplemental oxygen with assisted ventilation as required.
- Randomized, double-blind cross-over studies showed minimal efficacy of bronchodilators. This could be due to the absence of airway hyperresponsiveness in some

TDI-induced asthma.

EYE EXPOSURE

- DECONTAMINATION: Exposed eyes should be irrigated with copious amounts of tepid water for at least 15 minutes. If irritation, pain, swelling, lacrimation, or photophobia persist, the patient should be seen in a health care facility.

DERMAL EXPOSURE

- DECONTAMINATION: Wash exposed area extremely thoroughly with soap and water. A physician may need to examine the area if irritation or pain persists.

Range of Toxicity:

- Available dose-response information concerning humans pertains to inhalational exposure. Concentrations of 2.5 ppm are considered Immediately Dangerous to Life or Health. A fatality in an asthmatic who continued exposure to TDI has been reported.
- The recommended short term exposure limits for TDI in industry is 0.02 ppm. TDI does not have sufficient warning properties (e.g. odor or eye irritancy) at air concentrations below the recommended short term exposure limit.

[Rumack BH: POISINDEX(R) Information System. Micromedex, Inc., Englewood, CO, 2001; CCIS Volume 107, edition exp February, 2001. Hall AH & Rumack BH (Eds):TOMES(R) Information System. Micromedex, Inc., Englewood, CO, 2001; CCIS Volume 107, edition exp February, 2001.] **PEER REVIEWED**

Antidote and Emergency Treatment:

Noncardiogenic pulmonary edema and bronchospasm are the most immediate serious clinical consequences of isocyanate exposure. Markedly symptomatic patients should receive oxygen, ventilatory support, and an intravenous line. Treatment for asthma includes inhaled sympathomimetics (salbutamol, metaproterenol), intravenous theophylline, parenteral sympathomimetics (epinephrine, terbutaline), and steroids. /Isocyanates/

[Ellenhorn, M.J. and D.G. Barceloux. Medical Toxicology - Diagnosis and Treatment of Human Poisoning. New York, NY: Elsevier Science Publishing Co., Inc. 1988. 881]**PEER REVIEWED**

Copiously irrigate contaminated skin and eyes with saline. Few medical data are available to guide gut decontamination. Activated charcoal (1 g/kg) and a cathartic (sorbitol, magnesium citrate) may be useful for ingestions. /Isocyanates/

[Ellenhorn, M.J. and D.G. Barceloux. Medical Toxicology - Diagnosis and Treatment of Human Poisoning. New York, NY: Elsevier Science

Publishing Co., Inc. 1988. 881]**PEER REVIEWED**

Most treatment is symptomatic. Mydriatics, systemic analgesics, and topical antibiotics (Sulamyd) may be used for corneal abrasions. There is no effective therapy for sensitized workers, and these people should be moved to a work site devoid of exposure to isocyanates. /Isocyanates/
[Ellenhorn, M.J. and D.G. Barceloux. Medical Toxicology - Diagnosis and Treatment of Human Poisoning. New York, NY: Elsevier Science Publishing Co., Inc. 1988. 881]**PEER REVIEWED**

Any employee who begins to experience shortness of breath during a shift should be removed from work immediately and should not return to work until pulmonary function tests have returned to base line. As is the case with asthma of any type, pulmonary function recovery may lag behind symptom recovery and take up to eight weeks to return to normal. If sensitized, the individual should not return to work in a TDI area or work with any other isocyanate.
[Zenz, C. Occupational Medicine-Principles and Practical Applications. 2nd ed. St. Louis, MO: Mosby-Yearbook, Inc, 1988. 1020]**PEER REVIEWED**

Animal Toxicity Studies:

Evidence for Carcinogenicity:

No data are available in humans. Sufficient evidence of carcinogenicity in animals. OVERALL EVALUATION: Group 2B: The agent is possibly carcinogenic to humans.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. S7 72 (1987)]**PEER REVIEWED**

Non-Human Toxicity Excerpts:

THE POSSIBILITY OF DERMAL EXPOSURES TO **TOLUENE** DIISOCYANATE RESULTING IN PULMONARY SENSITIVITY WAS INVESTIGATED USING GUINEA PIGS AS AN ANIMAL MODEL. **TOLUENE** DIISOCYANATE (1-100% CONCN) WAS APPLIED TO DORSAL SITES ON GUINEA PIGS, WHERE SKIN SENSITIVITY TO TDI WAS APPARENT BY THE 7TH DAY. AFTER 14 DAYS, ANIMALS WERE ADDNL EVALUATED FOR TDI SENSITIVITY BY SEROLOGIC ANALYSIS & BRONCHIAL PROVOCATION CHALLENGE. ANTIBODIES TO **TOLUENE** DIISOCYANATE WERE DETECTED USING PASSIVE CUTANEOUS ANAPHYLAXIS, DOUBLE DIFFUSION IN GEL, & RADIOLABELED ANTIGEN BINDING ASSAYS. ANTIBODIES WERE SPECIFIC FOR **TOLUENE** DIISOCYANATE. THE DEVELOPMENT OF RESPIRATORY HYPERSENSITIVITY AS A RESULT OF DERMAL CONTACT WITH **TOLUENE** DIISOCYANATE EMPHASIZES THE IMPORTANCE OF CAREFUL WORKPLACE PRACTICES & SUGGESTS REEVALUATION OF THE ROLE OF INHALATION &/OR DERMAL CONTACT IN CAUSING PULMONARY SENSITIZATION OF WORKERS.
[KAROL MH ET AL; TOXICOL APPL PHARMACOL 58 (2): 221 (1981)]**PEER REVIEWED**

TOLUENE DIISOCYANATE WAS MUTAGENIC IN SALMONELLA TYPHIMURIUM STRAINS

TA1538 & TA98 AFTER METABOLIC ACTIVATION.
[ANDERSEN M ET AL; SCAND J WORK ENVIRON HEALTH 6 (3): 221 (1980)]**PEER REVIEWED**

GROUPS OF MALE & FEMALE RATS & MICE WERE EXPOSED TO 0.05 & 0.15 PPM OF 2,4/2,6-**TOLUENE**-DIISOCYANATE (80/20) BY INHALATION FOR 6 HR/DAY, 5 DAYS/WEEK FOR 2 YR. TYPE & INCIDENCE OF TUMORS & THE NUMBER OF TUMOR-BEARING ANIMALS OF EITHER SPECIES DID NOT INDICATE ANY CARCINOGENIC EFFECT. HEMATOLOGY, BIOCHEMISTRY, URINALYSIS, & CYTOGENICITY STUDIES DID NOT REVEAL ANY UNTOWARD EFFECT. INCREASED MORTALITY (FEMALES ONLY), REDUCED WEIGHT GAIN & SIGNS OF IRRITATION IN THE UPPER & LOWER RESPIRATORY TRACT RESULTED FROM EXPOSURE TO **TOLUENE** DIISOCYANATE IN THE MOUSE STUDY WITH THE HIGHEST INCIDENCE IN THE 0.15 PPM EXPOSURE LEVEL.
[LOESER E; TOXICOL LETT (AMST) 71 (1983)]**PEER REVIEWED**

EXPOSURE BY INHALATION TO 70 MG/CU M (10 PPM) ... 2,6-TDI OR 65/35 MIXT FOR 6 HR/DAY FOR 3-5 DAYS WAS LETHAL TO RATS; EXPOSURE TO 35 MG/CU M (5 PPM) OF MIXT FOR 4 DAYS KILLED 65% OF RATS.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V19 310 (1979)]**PEER REVIEWED**

LC50 FOLLOWING EXPOSURE ... FOR 14 DAYS WAS: MOUSE, 70 MG/CU M ... GUINEA PIG, 90 MG/CU M ... & RAT, 100 MG/CU M ... LC50 FOLLOWING EXPOSURE FOR 7 DAYS WAS 80 MG/CU M ... IN RABBITS. ... MICE, RATS & GUINEA PIGS EXHIBITED LACRIMATION, SALIVATION, RESTLESSNESS & HYPERACTIVITY.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V19 310 (1979)]**PEER REVIEWED**

ACUTE 6-HR INHALATION STUDIES IN RATS, CONCN OF 4200 MG/CU M ... WAS LETHAL, WHEREAS 420 MG/CU M ... WAS NOT. ANIMALS THAT DIED SHOWED ACUTE PULMONARY CONGESTION & EDEMA.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V19 310 (1979)]**PEER REVIEWED**

FOLLOWING EXPOSURE BY INHALATION ... TO 0.7 MG/CU M (0.1 PPM) ... FOR 6-HR ... 1 DAY/WK FOR 38 WK, OR ... 6 HR/DAY ON 5 DAYS/WK FOR ... 58 EXPOSURES, RAT SHOWED PROLIFERATION OF FIBROUS TISSUE ... OF BRONCHIOLES AS WELL AS PNEUMONITIS, TRACHEITIS & BRONCHITIS. IN RABBITS & GUINEA PIGS, NO PROLIFERATION ... .
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V19

310 (1979)]**PEER REVIEWED**

ACUTE SKIN ABSORPTION TESTS ... ON RABBITS PRODUCED SEVERE LOCAL IRRITATION BUT FAILED TO KILL, EVEN WITH DOSES AS HIGH AS 16 G/KG BODY WT ... NO ANATOMICAL INJURY TO INTESTINAL ORGANS.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V19 310 (1979)]**PEER REVIEWED**

TEST APPLICATION OF DROP OF META & PARA TOLUENEDIISOCYANATES ON RABBIT EYES CAUSED IMMEDIATE PAIN, LACRIMATION, SWELLING OF LIDS, & CONJUNCTIVAL REACTION. HOWEVER, CORNEAL EPITHELIUM WAS ONLY MILDLY DAMAGED ... /MIXT OF 2,4- & 2,6-ISOMERS/
[Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986. 929]**PEER REVIEWED**

EXPOSURE OF GUINEA PIGS BY INHALATION TO 14-35 MG/CU M (2-5 PPM) ... IN AIR ... 6 HR/DAY FOR 3 DAYS RENDERED THEM MORE SENSITIVE WHEN 3 WK LATER THEY WERE EXPOSED TO 0.14 MG/CU M (0.02 PPM) FOR 5 HR, AS SHOWN BY MORE PRONOUNCED REDN OF BREATH RATE ... COMPARED WITH ANIMALS ... NOT ... PREVIOUSLY EXPOSED.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V19 310 (1979)]**PEER REVIEWED**

Groups of 120 male and 120 female CD-1 mice, three to four weeks old, were exposed to 0, 0.05, or 0.15 ppm (0, 0.36 or 1.07 mg/cu m) production grade **toluene** diisocyanate (approx 80% 2,4 isomer & 20% 2,6 isomer) in an inhalation chamber for 6 hr/day on 5 days/wk for 104 wk. There was a significant reduction in body weight in the high-dose group /sex not stated/ and a significant increase in mortality in both high and low-dose females by the termination of the study. No such effect was seen in males. Neither the types of tumor observed nor their incidences were dose-related, and both corresponded to those seen in historical controls for this strain of mice. However, dose-related pathological changes were observed in the nasal cavity (chronic or necrotic rhinitis), together with changes in the lower respiratory tract (interstitial pneumonia, catarrhal bronchitis) in both groups.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 303 (1986)]**PEER REVIEWED**

Groups of 126 male and 126 female Sprague Dawley CD rats, six to nine weeks old, were exposed to 0, 0.05 or 0.15 ppm (0, 0.36 or 1.07 mg/cu m) production-grade **toluene** diisocyanate (approx 80% 2,4 isomer and 20% 2,6 isomer) in an inhalation chamber for 6 hr/day on 5 days/wk for 108 wk or 110 wk. A significant reduction in weight gain was observed during the first 12 wk of the study among the high-dose animals of each sex, but body wt gain was similar in all groups thereafter. No significant difference in mortality between treated and control groups of either sex was reported. Tumor incidences and types were reported to be similar in control and treated groups.

[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 304 (1986)]**PEER REVIEWED**

Rats receiving up to 240 mg/kg **toluene** diisocyanate by gavage daily on 5 days/wk for 13 wk were found to suffer from mild to moderate bronchopneumonia.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 306 (1986)]**PEER REVIEWED**

In dogs, a correlation has been made between immunological and respiratory responses to **toluene** diisocyanate. Dogs exposed once every second week for 41 wk to 1 mg/kg **toluene** diisocyanate delivered as an aerosol intratracheally developed a systemic immune response to **toluene** diisocyanate conjugated with dog serum albumin as well as immediate-type airway responses.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 307 (1986)]**PEER REVIEWED**

The **toluene** diisocyanate induced delayed type hypersensitivity reaction in the ear of male mice was investigated and compared with the picryl chloride induced one. The results obtained were as follows: 1) When 1% **toluene** diisocyanate solution (20 ul/ear) as a challenging concentration was used for 7 week old ICR mice, distinct ear swelling was observed in every group sensitized with various concentrations (1-5%, 100 ul/animal) of **toluene** diisocyanate solution, and the swelling rate was the same or higher than that of picryl chloride induced delayed type hypersensitivity. 2) Five, 7 and 13 week old ICR mice showed a similar high response in TDI induced delayed type hypersensitivity, whereas the reactivity of 16 week old ICR mice was significantly lower than that of the above mentioned younger mice. 3) In both **toluene** diisocyanate and picryl chloride induced delayed type hypersensitivity reaction, ICR and BALB/c mice showed a similar high response, whereas the reactivity of ddY mice was significantly lower. The effects of dexamethasone and indomethacin were investigated with the **toluene** diisocyanate induced delayed type hypersensitivity model. The delayed type hypersensitivity reaction was suppressed significantly by both drugs, but the suppressive effects of dexamethasone were higher than that of indomethacin. All the above results indicate that the **toluene** diisocyanate induced delayed type hypersensitivity model in mice taking dye leakage as an index may be useful for evaluation of drugs for disorders derived from delayed type hypersensitivity reactions.
[Tominaga M et al; Jpn J Pharmacol 39 (2): 163-71 (1985)]**PEER REVIEWED**

Exposing guinea pigs to **toluene** diisocyanate causes an acute increase in airway responsiveness to inhaled acetylcholine. The mechanism of this increase in airway responsiveness is unknown. Capsaicin-sensitive afferent nerves and the tachykinins they release upon activation are important in controlling bronchomotor tone in guinea pigs. To determine whether tachykinins are important in **toluene** diisocyanate induced airway hyperresponsiveness, the effects of tachykinin depletion were studied using capsaicin, and competitive tachykinin antagonism, using (D-Argl, D-Pro2, D-Trp7.9, Leull) substance P, on **toluene** diisocyanate induced airway hyperresponsiveness. In 9 of 9 untreated

animals, **toluene** diisocyanate exposure caused a large and significant increase in airway responsiveness to acetylcholine. The mean concentration of acetylcholine required to decrease specific airway conductance by 50% below baseline (the PD50) was 1.51% before **toluene** diisocyanate exposure and 0.17% after **toluene** diisocyanate exposure ($p < 0.0005$). Capsaicin treatment had no effect on the PD50 but prevented the **toluene** diisocyanate induced increase in airway responsiveness in 10 of 12 animals. (The PD50 was 1.03% before **toluene** diisocyanate and 1.27% after **toluene** diisocyanate exposure.) Treatment with the tachykinin antagonist (D-Argl, D-Pro2, D-Trp7.9, Leull) substance P also abolished the **toluene** diisocyanate induced increase in airway responsiveness in all 5 animals treated. Although **toluene** diisocyanate exposure also caused airway edema, the effect of capsaicin treatment on **toluene** diisocyanate induced hyperresponsiveness did not result from prevention of airway edema. **Toluene** diisocyanate exposure caused a marked increase in tracheal extravasation of intravenously administered Evans blue dye that was not prevented by capsaicin treatment.
[Thompson JE et al; Am Rev Respir Dis 136 (1): 43-9 (1987)]**PEER REVIEWED**

The changes in airway responsiveness to increasing doses of an acetylcholine aerosol in anesthetized and ventilated guinea pigs 2, 6, or 24 hr after exposure to air or 1 ppm **toluene** diisocyanate were examined. Pulmonary resistance after the animals inhaled a buffered saline aerosol was used as baseline and was similar for air and groups. The concentration of acetylcholine calculated to cause a 200% increase in pulmonary resistance was significantly lower for animals studied at 2 hr (0.68%) or at 6 hr (0.77%), but not at 24 hr (2.39%), after than for air animals (3.07%). The increase in airway responsiveness in the exposed animals was associated with histologic changes in the trachea and intrapulmonary airways. Exposure to 2 ppm caused a patchy loss of cilia, shedding of epithelial cells into the airway lumen, and an influx of inflammatory cells into the trachea and other airways. In the lamina propria of the trachea, the concentration of extravascular polymorphonuclear leukocytes was 13 to 26-fold greater in animals studied 2 or 6 hr after exposure to 2 ppm **toluene** diisocyanate or at 2 hr after 1 ppm **toluene** diisocyanate than in animals exposed to air. The concentration of polymorphonuclear leukocytes in the epithelium was significantly increased only in animals examined 2 hr after 2 ppm **toluene** diisocyanate. Exposure to **toluene** diisocyanate also caused an influx of eosinophils into the tracheal mucosa. This influx occurred later and was more persistent than the influx of polymorphonuclear leukocytes. These results indicate that a single exposure to **toluene** diisocyanate can cause an increase in airway responsiveness that is associated with epithelial injury and acute airwayinflammation.
[Gordon T et al; Am Rev Respir Dis 132 (5): 1106-12 (1985)]**PEER REVIEWED**

The effect of exposure to **toluene** diisocyanate vapor on pulmonary performance was studied in guinea pigs. Female English smooth haired guinea pigs were exposed to 1.4 ppm **toluene** diisocyanate vapor or air for 3 hours per day for 4 days, or to 0.02 ppm **toluene** diisocyanate for 6 hours per day for 70 days. Pulmonary performance was evaluated by the ventilatory response of the animals to 10% carbon dioxide. Serum antibodies to **toluene** diisocyanate were measured on days 22 and 50 and **toluene** diisocyanate pulmonary hypersensitivity was measured on days 37 and 38. Lung tissue histopathology was evaluated in all animals on day 50 following **toluene** diisocyanate exposure. Pulmonary response to 10% carbon dioxide diminished by 30 to 50% following **toluene** diisocyanate exposures at 1.4 ppm up to day 14. The ventilatory response showed recovery during the next 5 weeks. In contrast, animals exposed to 0.02 ppm **toluene** diisocyanate daily for 70 days showed no change in ventilatory response, nor did control animals that were not exposed to **toluene** diisocyanate. Antibodies were detected on day 22 and pulmonary

hyprsensitivity to **toluene** diisocyanate was found in all animals exposed to 1.4 ppm **toluene** diisocyanate. No antibodies to **toluene** diisocyanate nor pulmonary hypersensitivity were detected in animals exposed to 0.02 ppm **toluene** diisocyanate or in control animals. Lung tissue on day 50 in the 1.4 ppm **toluene** diisocyanate exposed animals showed multifocal subchronic interstitial inflammation, localized pleural thickening, and peripheral lymphoid hyperplasia. No apparent abnormalities were observed in lung tissue of the 0.02 ppm exposed group. Exposure to 1.4 or 0.02 ppm **toluene** diisocyanate resulted in measurable and no apparent pulmonary toxicity in guinea pigs, respectively. The 10 percent carbon dioxide challenge provide several advantages for measuring pulmonary function.
[Wang KL et al; J Toxicol Environ Health 15 (1): 137-48 (1985)]**PEER REVIEWED**

Groups of 50 F344/N rats of each sex and 50 B6C3F1 mice of each sex were gavaged with corn oil or a mixture of **toluene** diisocyanate in corn oil for 5 days per wk for 105 or 106 wk. Female rats and mice were given doses of 60 or 120 mg/kg body weight, while male rats received 30 or 60 mg/kg, and male mice received 120 or 240 mg/kg. The **toluene** diisocyanate reacted with the moisture in the corn oil vehicle resulting in doses that were 10% to 23% below the target dose concn. The chemical product used was commercial grade **toluene** diisocyanate, which was an 80%-20% mixture of the 2,4- and 2,6-isomers. Chemical disposition and metabolism studies were conducted with each of the radiolabelled **toluene** diisocyanate isomers in male rats. Absorption of both of the **toluene** diisocyanate isomers occurred, with the highest concn found in the stomach, cecum, large intestine, and bladder. Excretion occurred via the feces and urine. The major metabolic products from the metabolism of 2,4-**toluene** diisocyanate were shown to be identical with those from the metabolism of the carcinogen, 2,4-diaminotoluene, whereas the metabolism of the 2,6-**toluene** diisocyanate isomer yielded one major product, identified as 2,6-bis(acetylamino)**toluene**. Greater than 10% depression in body weight gain occurred in all dosed groups of rats throughout most of the study. The major non-neoplastic lesions that were observed in both sexes of the **toluene** diisocyanate exposed rats were dose related incr in acute broncho-pneumonia, characterized as chemical pneumonitis, with incidences as high as 50%. In mice mean body weight gain was depressed in dosed male and in high dose females. The principle non-neoplastic lesion in mice that was attributed to chemical treatment was cytomegaly of the kidney tubular epithelium in males. Survival in all groups of dosed rats was significantly lower than in controls. A dose-dependent pattern of mortality did not commence until 70 wk of exposure, demonstrating that **toluene** diisocyanate elicited a cumulative toxic response. There was also significantly lower survival in high dose male, but not female mice, by comparison to controls. Despite the reduction of power and sensitivity in the rat studies caused by early mortality, statistically significant incr in tumor incidences were observed in many different target organs. **Toluene** diisocyanate was carcinogenic in F344/N rats, causing sc fibromas and fibrosarcomas in males and females, pancreatic acinar cell adenomas in males, and pancreatic islet cell adenomas, neoplastic nodules of the liver, and mammary gland tumors in females.
[Dieter MP et al; Toxicol Ind Health 6 (6): 599-621 (1990)]**PEER REVIEWED**

Toluene diisocyanate is a causative agent in occupational asthma. Through an oral catheter **toluene** diisocyanate, 0.03 ul, dissolved in 0.02 ml olive oil, was superfused on the tracheobronchial mucosa of anaesthetized guinea pigs. **Toluene** diisocyanate induced plasma exudation into both airway tissue and lumen (peak effect: 5 hr; duration approximately 17 hr). Light microscopy examinations demonstrated that the epithelium was not disrupted by this process (and that microvessels are abundant just beneath the

epithelium). At days 6 and 21 after exposure to **toluene** diisocyanate PAS-positive cells were increased, but no other histological alterations were found. Also, the occurrence of peptide containing nerve fibres was not altered by **toluene** diisocyanate. After **toluene** diisocyanate exposure the airway smooth muscle tone was elevated as examined in vitro at base-line and at conc response to carbachol. The largest incr in tone were recorded 21 days after exposure to **toluene** diisocyanate. The abnormally large tone was not associated with an increased thickness of the smooth muscle layer nor was it associated with reduced effects of either beta 2-agonist (terbutaline) or xanthine (theophylline) relaxants. It is concluded that **toluene** diisocyanate induced plasma exudation into guinea pig airways for 17 hr without disrupting the epithelial lining and without causing major changes in the airway peptidergic innervation. Both the airway tone, and the number of mucous cells, are increased for at least 3 wk after exposure to **toluene** diisocyanate.
[Persson CG et al; Clin Exp Allergy 21 (6): 715-24 (1991)]**PEER REVIEWED**

Toluene diisocyanate was mutagenic in Salmonella typhimurium strains TA98 and TA100 in the presence (but not the absence) of Aroclor 1254-induced male Sprague Dawley rat or male Syrian hamster liver S9; it was not mutagenic in strains TA 1535 or 1537.
[DHHS/NTP; Toxicology and Carcinogenesis Studies of Commercial Grade 2,4 (80%) and 2,6 (20%) - Toluene Diisocyanate (Gavage Studies) p. 7 (1986) Technical Rpt Series No. 251 NIH Pub No. 86-2507]**PEER REVIEWED**

National Toxicology Program Studies:

Groups of 50 female F344/N rats and 50 female B6C3F1 mice were administered commercial grade **toluene** diisocyanate (80% 2,4- and 20% 2,6-) in corn oil by gavage at doses of 60 or 120 mg/kg body weight, 5 days per week for 105 or 106 weeks. Groups of 50 male F344/N rats received 30 or 60 mg/kg and groups of 50 male B6C3F1 mice received 120 or 240 mg/kg on the same schedule. Dosage analyses of **toluene** diisocyanate indicated that the chemical had reacted in the corn oil vehicle, resulting in actual gavage concentrations 77% to 90% of theoretical values. Groups of 50 rats and 50 mice of each sex received corn oil only and served as vehicle controls. Survival in all groups of dosed rats in the 2-year studies was shorter (P less than or equal to 0.005) than that of the controls; depressions in mean body weight gain relative to controls were greater than 10% in all dosed rat groups throughout most of the study. A dose-dependent pattern of cumulative toxicity began at 70 weeks and culminated in excessive mortality, indicating the estimated maximum tolerated dose had been exceeded for rats. Acute bronchopneumonia occurred at increased incidences in groups of dosed male and female rats (males: control, 2/50; low dose, 6/50; high dose, 14/50; females: 1/50, 10/50, 25/49). /Results indicated that/ commercial grade **toluene** diisocyanate in corn oil was carcinogenic for F344/N rats, causing subcutaneous fibromas and fibrosarcomas (combined) in males and females, pancreatic acinar cell adenomas in males, and pancreatic islet cell adenomas, neoplastic nodules of the liver, and mammary gland fibroadenomas in females. **Toluene** diisocyanate was not carcinogenic for male B6C3F1 mice. TDI was carcinogenic for female B6C3F1 mice, causing hemangiomas or hemangiosarcomas (combined), as well as hepatocellular adenomas.
[DHHS/NTP; Toxicology and Carcinogenesis Studies of Commercial Grade 2,4 (80%) and 2,6 (20%) - Toluene Diisocyanate (Gavage Studies) p. 7 (1986) Technical Rpt Series No. 251 NIH Pub No. 86-2507]**PEER REVIEWED**

Non-Human Toxicity Values:

LC50 Rat inhalation 56.96 mg/cu m/1 hr
[WHO; Environmental Health Criteria 75: Toluene Diisocyanates p. 33 (1987)]**PEER REVIEWED**

LC50 Rat inhalation 98.96 + or - 8.6 mg/cu m/4 hr
[WHO; Environmental Health Criteria 75: Toluene Diisocyanates p. 33 (1987)]**PEER REVIEWED**

LC50 Rat (male) inhalation 348.88 mg/cu m/4 hr
[WHO; Environmental Health Criteria 75: Toluene Diisocyanates p. 33 (1987)]**PEER REVIEWED**

LC50 Rat (female) inhalation 356 mg/cu m/4 hr
[WHO; Environmental Health Criteria 75: Toluene Diisocyanates p. 33 (1987)]**PEER REVIEWED**

LC50 Mouse inhalation 69.1 + or - 9.96 mg/cu m/4 hr
[WHO; Environmental Health Criteria 75: Toluene Diisocyanates p. 33 (1987)]**PEER REVIEWED**

LC50 Rabbit inhalation 78.32 mg/cu m/4 hr
[WHO; Environmental Health Criteria 75: Toluene Diisocyanates p. 33 (1987)]**PEER REVIEWED**

LC50 Guinea pig inhalation 90.4 + or - 19.2 mg/cu m/4 hr
[WHO; Environmental Health Criteria 75: Toluene Diisocyanates p. 33 (1987)]**PEER REVIEWED**

LD50 Rat oral 3060 mg/kg
[WHO; Environmental Health Criteria 75: Toluene Diisocyanates p. 33 (1987)]**PEER REVIEWED**

Metabolism/Pharmacokinetics:

Metabolism/Metabolites:

A technique for detectingurinary amine metabolites in rats exposed to **toluene** diisocyanate was evaluated. Skin tissue of rats was exposed to 40% **toluene**-2,4-diisocyanate solution in di-n-butyl-ether liquid. Rats were exposed daily for 3 hr on 4 consecutive days. Urine was collected in metabolic cages for 18 hr after the last exposure. Chromatographic techniques were used for nitrogen selective detection of nonderivatized amines. An autolinear temperature programmer was employed to analyze derivatized amine. The identity of the amine was confirmed by gas chromatography/mass spectrometry. A linear correlation was found between **toluene**-2,4-diamine added to urine and peak height. Peak height and recovery from the non hydrolyzed and from the hydrolyzed urine was about 85 and 70%, respectively. No free **toluene**-2,4-diamine or free **toluene**-2,4-diisocyanate was detected in the urine of rats exposed to **toluene**-2,4-diamine in hydrolyzed urine was 1.5 micrograms per milliliter. Gas chromatography/mass spectrometry confirmed the identity of the amine. /This/ highly sensitive technique tested is easy to apply

and is effective for trace assays of amines.
[Rosenberg C; J Chromatography 323 (2): 429-33 (1985)]**PEER REVIEWED**

Epithelial injury and inflammation are involved in airway hyperresponsiveness and asthma induced by **toluene** diisocyanate. In that isocyanates are insoluble and highly reactive compounds, bronchial epithelial cells may represent the most important target cells of their toxic effect. We hypothesized that damage to airway epithelium by **toluene** diisocyanate may result in the release of metabolites of arachidonic acid, which are known to promote inflammation and to alter epithelial cell function and airway smooth muscle responsiveness. To test this hypothesis we examined eicosanoid products in the culture media of bronchial epithelial cells exposed in vitro to 8 and 18 ppb **toluene** diisocyanate. Epithelial cells derived from human bronchi obtained at surgery were cultured to confluency on collagen-coated microporous membranes. Those cells, which expressed differentiated characteristics of epithelial cells (they showed keratin-containing filaments and had a cobblestone appearance), were alternatively exposed to **toluene** diisocyanate or air for 30 min in a specially designed in vitro chamber. The production of metabolites of arachidonic acid was assessed by measuring the release of immunoreactive products into the cell medium at the end of the exposure and during a 2 hr period after exposure. This method revealed a predominant isocyanate induced release of immunoreactive 15-hydroxyeicosatetraenoic acid. Release rate of this compound tended to be dose-related and was associated with cell damage as assessed by the release of lactate dehydrogenase in the medium.
[Mattoli S et al; J Cell Physiol 142 (2): 379-85 (1990)]**PEER REVIEWED**

It has been previously shown that tachykinin depletion or antagonism prevented the increase in airway responsiveness to inhaled acetylcholine caused by exposure to **toluene** diisocyanate in awake guinea pigs. To insure that the effects of tachykinins were not limited to the extrathoracic airways and were not dependent on effects of **toluene** diisocyanate on baseline airway caliber, airway responsiveness to acetylcholine inhaled through tracheostomy in anesthetized and ventilated guinea pigs that were exposed to **toluene** diisocyanate or air after treatment with the tachykinin antagonist spantide, the tachykinin metabolism inhibitor phosphoramidon, or the vehicles for each drug were determined. When these drugs were administered before and during **toluene** diisocyanate exposure, spantide significantly inhibited the **toluene** diisocyanate induced increase in acetylcholine responsiveness and phosphoramidon significantly potentiated this effect, whereas neither drug altered acetylcholine responsiveness in air exposed animals. To determine whether tachykinins were exerting their effect primarily during **toluene** diisocyanate exposure or during the subsequent acetylcholine challenge, the effect of each drug on acetylcholine responsiveness was also examined when the drugs were given after **toluene** diisocyanate exposure. At that time, spantide did not inhibit **toluene** diisocyanate induced acetylcholine hyperresponsiveness and phosphoramidon did not potentiate it. Neither drug nor **toluene** diisocyanate increased pulmonary resistance measured through a tracheostomy in these anesthetized and ventilated animals. These results suggest that the **toluene** diisocyanate induced increase in acetylcholine responsiveness is mediated by release of tachykinins into the intrathoracic airways during exposure to **toluene** diisocyanate.
[Sheppard D, Scypinski L; Am Rev Respir Dis 138 (3): 547-51 (1988)]**PEER REVIEWED**

Five men were exposed to **toluene** diisocyanate atmospheres for 7.5 hr. The **toluene** diisocyanate atmospheres were generated by a gas-phase permeation method, and the exposures were performed in an 8 cu m stainless steel test chamber. The mean air concn of **toluene** diisocyanate was ca 40 ug/cu m,

which corresponds to the TLV of Sweden. The inhaled doses of 2,4- and 2,6-**toluene** diisocyanate were ca 120 ug. **Toluene** diisocyanate in the test chamber air was determined by an HPLC method using the 9-(N-methylaminomethyl)-anthracene reagent and by a continuous monitoring filter-tape instrument. After hydrolysis of plasma and urine, the related amines, 2,4- and 2,6-toluenediamine 2,4-, and 2,6-TDA), were determined as pentafluoropropionic anhydride derivatives by capillary gas-chromatography using selected ion monitoring in the electron-impact mode. The urinary elimination of the toluenediamines showed a possible biphasic pattern, with rapid first phases for 2,4-toluenediamine (mean half-life for the concn in urine, 1.9 hr) and for 2,6-toluenediamine (mean half-life for the concn in urine, 1.6 hr). The cumulative amount of 2,4-toluenediamine excreted in urine within 28 hr ranged from 8% to 14% of the estimated dose of 2,4-**toluene** diisocyanate, and the cumulative amount of 2,6-toluenediamine in urine ranged from 14% to 18% of the 2,6-**toluene** diisocyanate dose. The average urinary level of 2,4-toluenediamine was 5 ug/l in the 6 to 8 hr sample (range 2.8-9.6 ug/l), and the corresponding value fo 2,6-toluenediamine was 8.6 ug/l (range, 5.6-16.6 ug/l). Biological monitoring of exposure to 2,4- and 2,6-**toluene** diisocyanate by analysis of 2,4- and 2,6-toluenediamine in urine is feasible.
[Skarping G et al; Int Arch Occup Environ Health 63 (2): 83-8 (1991)]**PEER REVIEWED**

Mechanism of Action:

SERUM FROM 26 PERSONS SHOWN TO REACT TO PROVOCATIVE INHALATION CHALLENGE WITH LOW CONCN OF **TOLUENE** DIISOCYANATE WAS TESTED BY RADIOALLERGOSORBENT TEST (RAST) USING A P-TOLYL ISOCYANATE-HUMAN SERUM ALBUMIN (TMI-HSA) CONJUGATE. POSITIVE RESULTS WERE OBTAINED IN 15-19% OF **TOLUENE** DIISOCYANATE REACTORS, DEPENDING ON THE METHOD OF EVALUTION. **TOLUENE** DIISOCYANATE ASTHMA MAY BE A COMPLEX SYNDROME WITH SEVERAL TYPES OF REACTIONS POSSIBLE, INCLUDING AN IMMUNOGLOBULIN-E MECHANISM IN SOME INDIVIDUALS. THE THEORY THAT **TOLUENE** DIISOCYANATE ASTHMA IS BASED SOLELY ON AN IMMUNE MECHANISM IS NOT SUPPORTED. THE FINDINGS DO NOT DISAGREE WITH THE HYPOTHESIS THAT **TOLUENE** DIISOCYANATE REACTIVITY MAY BE MEDIATED BY A PHARMACOLOGIC MECHANISM.
[BUTCHER BT ET AL; J ALLERGY CLIN IMMUNOL 66 (3): 213 (1980)]**PEER REVIEWED**

To investigate the role of pharmacological mechanisms in **toluene** diisocyanate induced occupational asthma, the effects of **toluene** diisocyanate on rat trachea ring and lung parenchymal strip were studied in vitro. The most prominent effect observed was a stimulation of metacholine induced contraction of the tracheal ring by 1M **toluene** diisocyanate (added in dimethyl sulfoxide). The results were less pronounced when **toluene** diisocyanate was added from a stock solution prepared in water, which is possibly due to copolymerisation. It is concluded that the pharmacological effect of **toluene** diisocyanate may result from an autonomic imbalance between cholinergic and B-adrenergic neural control.
[Borm PJA et al; Br J Ind Med 46 (1): 56-9 (1989)]**PEER REVIEWED**

A study of the occurrence of serum immunoglobulin-E and immunoglobulin-G antibodies in workers with isocyanate induced asthma was conducted. The study group consisted of 62 workers (58 males) being evaluated for occupational asthma. Thirty nine had been exposed to hexamethylene diisocyanate, 17 to diphenylmethane diisocyanate, and six to **toluene** diisocyanate. The subjects completed a

respiratory and occupational questionnaire. Spirometric tests were administered. Skin prick tests were performed with 15 common inhalant allergens and **toluene** diisocyanate, hexamethylene diisocyanate, and diphenylmethane diisocyanate human serum albumin conjugates. Blood samples were collected and assayed for specific serum immunoglobulin-G and immunoglobulin-E antibodies to hexamethylene diisocyanate, diphenylmethan diisocyanate, and **toluene** diisocyanate. Specific inhalation challenges were conducted with hexamethylene diisocyanate, diphenylmethane diisocyanate, and **toluene** diisocyanate. Specific inhalation challenge with **toluene** diisocyanate, hexamethylene diisocyanate, or diphenylmethane diisocyanate induced significant bronchoconstriction in half of the subjects, late reactions being the most common. Twenty subjects had significantly elevated immunoglobulin-G concn and nine had significantly elevated immunoglobulin-G plus immunoglobulin-E concn. Six of 12 subjects with elevated immunoglobulin-E and immunoglobulin-G antibodies had positive skin prick tests for hexamethylene diisocyanate and one was sensitized to diphenylmethane diisocyanate. It was concluded that an association between isocyanate specific antibodies and the results of specific inhalation challenge tests has been established. This suggests that isocyanate induced asthma may involve an immunological mechanism.
[Cartier A et al; J Allergy Clin Immunol 84 (4 Part 1): 507-14 (1989)]**PEER REVIEWED**

The influence of cyclophosphamide induced granulocyte depletion on **toluene** diisocyanate related changes in airway reactivity and pathology was assessed in guinea pigs. Twelve cyclophosphamide-treated and 12 control animals comprising each group were studied physiologically before and 2 hr after a single 10 min exposure to 3 ppm of **toluene** diisocyanate. Reactivity was determined in intact unanesthetized animals by measuring specific airway conductance before and during intravenous acetylcholine infusion. After testing, tracheal tissue for light microscopic examination was obtained from three hyperreactive guinea pigs in each exposed group and compared with tissue from treated and control animals (n = 3 each) that had not been **toluene** diisocyanate exposed. Cyclophosphamide treatment caused substantial decr in both circulating and airway granulocyte counts. However, the incidence and degree of bronchial hyperreactivity that occurred 2 hr post-**toluene** diisocyanate was similar in the untreated and treated groups. Results indicate that **toluene** diisocyanate induced bronchial hyperreactivity 1) occurs shortly after a brief high concn exposure and 2) appears independent of circulating or airway granulocyte counts.
[Cibulas W Jr et al; J Appl Physiol 64 (5): 1773-8 (1988)]**PEER REVIEWED**

To determine the importance of airway inflammation for the development of late asthmatic reactions, we examined sensitized subjects during late asthmatic reactions induced by exposure to **toluene** diisocyanate in the laboratory. Late asthmatic reactions are associated with a transient increase of bronchial responsiveness and, at the same time, with an increase of neutrophils followed by eosinophils, and of leukotriene B4 and albumin in bronchoalveolar lavage fluid. Late asthmatic reactions, increased bronchial responsiveness, and increase of neutrophils, eosinophils, leukotriene B4, and albumin concn in bronchoalveolar lavage induced by exposure to **toluene** diisocyanate are all prevented by pretreatment with prednisone but not with the nonsteroidal anti-inflammatory agent indomethacin. Aerosolized steroids (beclomethasone and dexamethasone isonicotinate) completely inhibit late asthmatic reactions induced by **toluene** diisocyanate, whereas theophylline has a partial, and verapamil, ketotifen, and cromolyn have no protective effect. These results suggest that late asthmatic reactions induced by **toluene** diisocyanate may be caused by airway inflammation, and that anti-inflammatory steroids should

be recommended in the prophylaxis of **toluene** diisocyanate asthma.
[Fabbri LM et al; Am Rev Respir Dis 143 (3 Pt 2): 537-8 (1991)]**PEER REVIEWED**

The effects of **toluene** diisocyanate on T-cell subpopulations and circulating lymphocytes in ten persons (five males)): 19 to 50 yr old, with **toluene** diisocyanate induced occupational asthma were examined. Five subjects revealed early and late asthmatic reactions to **toluene** diisocyanate (dual responders) and five revealed late asthmatic reactions (late responders). Subjects underwent inhalation challenge with 0.005 to 0.015 ppm **toluene** diisocyanate or filtered air for 10 to 30 min on two occasions. One second forced expiratory volumes were measured before and at periodic intervals between 30 min and 24 hr after challenge. Venous blood samples were drawn 30 min and 8, 24, 48, and 72 hr after **toluene** diisocyanate. Total and differential leukocyte counts and T-cell subpopulations were determined. The five dual responders demonstrated forced expiratory volume in 1 sec decreased indicative of early and late asthmatic reactions and the five late responders demonstrated forced expiratory volume in 1 second decr indicative of a late asthmatic reaction. **Toluene** diisocyanate challenge did not affect the number of circulating erythrocytes and leukocytes. The percentage of eosinophils was significantly increased 24 hr after challenge and sustained for up to 48 hr. The percentages of neutrophils, lymphocytes, and monocytes were not altered by **toluene** diisocyanate. Among the T-lymphocyte subpopulation, the proportion of CD8(+) lymphocytes was significantly increased 8 hr after **toluene** diisocyanate challenge. The increase was more pronounced in the lat responders. An additional increase in CD8(+) lymphocytes occurred 48 hr post exposure in seven subjects but was unrelated to responder type. The number of CD4(+) cells did not change. This resulted in a decrease in the CD4(+)/CD8(+) ratio 8 and 48 hr after **toluene** diisocyanate challenge. It was concluded that **toluene** diisocyanate induced late asthmatic reactions are associated with an increase in the number of suppressor/cytotoxic lymphocytes and eosinophils in peripheral blood.
[Finotto S et al; Br J Ind Med 48 (2):116-21 (1991)]**PEER REVIEWED**

Intravenously administered endotoxin inhibits the polymorphonuclear leukocyte dependent airway edema produced in guinea pigs exposed to **toluene** diisocyanate. Tumor necrosis factor is produced in vivo by peripheral blood monocytes and tissue macrophages stimulated with endotoxin and has been shown to activate polymorphonuclear leukocyte's and vascular endothelial cells. To determine whether the inhibition of airway edema is mediated by tumor necrosis factor, guinea pigs were treated with intravenous saline or 75,000 U/kg recombinant human tumor necrosis factor 1.5 hr before exposure to air or 3 ppm **toluene** diisocyanate for 1 hr. Animals were then injected intravenously with 50 mg/kg Evans blue dye as a marker of protein extravasation. Saline-treated animals exposed to **toluene** diisocyanate had a significant increase in tracheal Evans blue dye extravasation (85 + or - 6.5 ug dye/g trachea, mean + or - standard error) compared with saline-treated animals exposed to air (31.3 + or - 2.5, $P < 0.001$). The tracheal extravasation of Evans blue dye was significantly inhibited ($P < 0.05$) in **toluene** diisocyanate exposed animals treated with tumor necrosis factor (64.7 + or - 7.5). Neither heat-inactivated tumor necrosis factor (104.9 + or - 9.5) nor tumor necrosis factor neutralized with a monoclonal antibody against tumor necrosis factor (99.7 + or - 17.9) inhibited **toluene** diisocyanate induced airway edema. In addition, treatment with 15,000 U/kg (99.9 + or - 21.3) or 150,000 U/kg (103.2 + or - 17.6) interleukin 1, a monokine also produced in response to endotoxin, did not prevent airway edema. These results suggest that tumor necrosis factor released in response to endotoxin mediates endotoxin's inhibition of a polymorphonuclear leukocyte dependent airway edema.
[Gordon T, Sheppard D; J Appl Physiol 64 (4): 1988 1688-92]**PEER

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Serum immunoglobulin-G and immunoglobulin-E to isocyanate haptenized human serum albumin (HSA) were estimated by ELISA in 55 isocyanate workers who underwent isocyanate inhalation challenge studies in Montreal, Canada. The challenges were negative in 29 workers and positive in 26 workers. Isocyanate antibodies were estimated by ELISA index. The mean immunoglobulin-G indices were found to be significantly higher in the challenge-positive workers, and there was a similar trend for the immunoglobulin-E indices. Antibody specificities for **toluene** diisocyanate-human serum albumin, diphenylmethane diisocyanate-human serum albumin, and hexamethylene diisocyanate-human serum albumin were determined by inhibition studies with a variety of isocyanate haptenized carriers. The other isocyanate substituted carriers were either noninhibitory or caused only partial inhibition as contrasted with the complete inhibition achieved by human serum albumin conjugated to the isocyanate to which the worker was exposed. We interpret these specificity studies as indicating that the inhalation of isocyanates results in production of antibody that recognizes new antigenic determinants that develop from the coupling of isocyanates to homologous proteins.
[Grammer LC et al; J Allergy Clin Immunol 86 (1): 94-8 (1990)]**PEER REVIEWED**

Inhalation of **toluene** diisocyanate results in toxic responses ranging from pulmonary irritation to immunological sensitization. The use of radioactively labeled isocyanate has made it possible to follow the initial uptake of the compound into the bloodstream independent of the final fate of the isocyanate. This study shows that the rate of uptake into the blood is linear during exposure to concn ranging from 0.00005 to 0.146 ppm and that the uptake continues to increase slightly postexposure. It also demonstrates that the radioactivity clears from the bloodstream to a level corresponding to approximately a 100 nM concn of tolyl group after 72 hr and persists at a nanomolar level even 2 wk following the exposure. The initial rate of (14)C uptake is also a linear function of the concn of **toluene** diisocyanate when expressed either as concn (ppm) or as concn multiplied by duration of exposure (ppm.hr). This is discussed in comparison with the toxic responses as a function of both ppm and ppm.hr. Finally, the inclusion of the data on methyl isocyanate indicates that the uptake into arterial blood is a function of exposure concn, independent of isocyanate structure.
[Kennedy AL et al; Toxicol Appl Pharmacol 100 (2): 280-92 (1989)]**PEER REVIEWED**

Isocyanates are an important cause of occupational asthma. The mechanism of isocyanate induced asthma is still unknown. To determine whether **toluene** diisocyanate stimulates the 'efferent' function of peripheral endings of capsaicin-sensitive sensory nerves, we investigated the effect of **toluene** diisocyanate in the rat isolated urinary bladder, a preparation in which the action of capsaicin has been well characterized. **Toluene** diisocyanate (0.03 mM) produced a concn dependent contraction of the bladder strips. It maximal effect was about 50 % of the response to capsaicin (1 uM). Previous exposure of the strips to capsaicin followed by washing out produced complete unresponsiveness, both to the first exposure to **toluene** diisocyanate and to a second exposure of capsaicin. Further, the response to both **toluene** diisocyanate and capsaicin was completely prevented by extrinsic bladder denervation, achieved by bilateral removal of pelvic ganglia (72 hr before). Repeated exposure of the rat bladder to **toluene** diisocyanate reduced the capsaicin-evoked release of calcitonin gene-related peptide like immunoreactivity (CGRP-LI), taken as biochemical marker of activation of these sensory nerves. These experiments provide the first evidence that **toluene** diisocyanate activates directly or indirectly the efferent function of capsaicin-sensitive primary sensory nerves.

[Mapp CE et al; Eur J Pharmacol 180 (1): 113-8 (1990)]**PEER REVIEWED**

The in vivo exposure to an asthmogenic stimulus, **toluene** diisocyanate, causes airway epithelial damage associated with inflammation and increased bronchial hyperresponsiveness. The latter mechanisms might partly be mediated by the release of eicosanoids from bronchial epithelial cells. Previously it has been demonstrated that the in vitro exposure of bronchial epithelial cells to **toluene** diisocyanate results in the release of immunoreactive 15-hydroxyeicosatetraenoic acid, a product of activation of the 15-lipoxygenase pathway with inflammatory properties. Present study shows that **toluene** diisocyanate induced release of 15-hydroxyeicosatetraenoic acid from epithelial cells can be prevented by nedocromil sodium, an anti-asthmatic drug with anti-inflammatory properties. This mode of action of the compound may explain its clinical effectiveness in asthma.

[Mattoli S et al; Int Arch Allergy Appl Immunol 92 (1): 16-22 (1990)]**PEER REVIEWED**

To determine whether early and/or late asthmatic responses induced by **toluene** diisocyanate are caused by a reflex mechanism involving stimulation of muscarinic receptors, we studied the effect of the muscarinic antagonist atropine on early and late airway response induced by **toluene** diisocyanate. A preliminary study was conducted in asthmatics to assess whether the selected dose of atropine provided adequate muscarinic blockade. On different days we measured the provocation dose (in mg) of carbachol causing a 15% decrease in forced expiratory volume in 1 second (PD15FEV1) without and with atropine premedication (0.008 or 0.012 mg/kg sc atropine 30 or 90 min before carbachol challenge test). 0.008 to 0.012 mg/kg sc atropine increased the PD15FEV1 carbachol by 6 to 10 fold, inducing a consistent and prolonged decrease in nonspecific bronchial hyperresponsiveness to cholinergic agent. 10 Subjects with a history of sensitization to **toluene** diisocyanate were then examined in 2 sets of experiments. In the first set of experiments, the subjects were studied before and after exposure to **toluene** diisocyanate (0.04 ppm; 30 min) after no treatment. In the second set of experiments, carried out 1 to 2 wk later, the same procedure was repeated after treatment with atropine (0.008 to 0.012 mg/kg atropine sulfate administered sc 30 min before **toluene** diisocyanate challenge, and then at 90 min intervals after **toluene** diisocyanate exposure); all patients showed symptoms of atropine effect (dryness of mouth, cycloplegia, increased heart rate).

[Paggiaro P et al; Am Rev Respir Dis 136 (5): 1237-41 (1987)]**PEER REVIEWED**

Light and electron microscopic structure of lobar bronchial biopsies were examined of nine subjects with occupational asthma induced by **toluene** diisocyanate and of four control nonasthmatic subjects who had never been exposed to **toluene** diisocyanate. Inflammatory cell numbers were separately assessed in the intact epithelium, in the more superficial layer of the submucosa, and in the total submucosa. Asthmatic subjects had an increased number of inflammatory cells in the airway mucosa compared with control subjects. Eosinophils were significantly increased in all compartments, CD45-positive cells were significantly increased in the epithelium and in the more superficial layer of the submucosa, and mast cells were significantly increased only in epithelium. By electron microscopy eosinophils and mast cells appeare degranulated only in asthmatic patients. In the areas of epithelium that appeared intact by light microscopy, electron microscopy showed that, although the intercellular spaces between columnar cells were similar in asthmatic and control groups, the intercellular spaces between basal cells were significantly wider in patients with asthma. Patients with **toluene** diisocyanate induced asthma also had a thicker subepithelial reticular layer, where immunohistochemistry showed the presence of collagen III. In

conclusion, in patients with asthma induced by **toluene** diisocyanate, the airway mucosa shows pathologic features, such as inflammatory cell infiltrate and thickening of subepithelial collagen, similar to those described in atopic asthma.
[Saetta M et al; Am Rev Respir Dis 145 (1): 160-8 (1992)]**PEER REVIEWED**

Serum neutrophil chemotactic activity, which is associated with mast cell or basophil activation, was quantitated to determine if mast cell or basophil mediators are released during bronchoprovocation-inhalation challenge with subirritant levels of **toluene** diisocyanate. Four subjects with suspected **toluene** diisocyanate induced asthma and four mite-sensitive subjects with asthma who served as a comparison group were studied. neutrophil chemotactic activity was measured in a multiwell, microchemotaxis chamber. Blood samples were collected, and forced expiratory volume in 1 second measurements were performed before challenge and at regular intervals during the subsequent 24 hr. Three of four workers clinically sensitive to **toluene** diisocyanate reacted to a subirritant **toluene** diisocyanate exposure. There was no increase in neutrophil chemotactic activity during placebo challenges. neutrophil chemotactic activity increased in the three **toluene** diisocyanate sensitive workers during early and late asthmatic reactions in quantities proportional to the forced expiratory volume in 1 second decline. No increase in neutrophil chemotactic activity was found during **toluene** diisocyanate exposures in the **toluene** diisocyanate negative worker. Gel filtration analysis demonstrated the main neutrophil chemotactic activity fraction eluted with macromolecules of an estimated molecular weight greater than 440,000 daltons. This characteristic is compatible with neutrophil chemotactic factor of basophil or mast cell origin. The kinetics of neutrophil chemotactic activity release were similar in mite- and **toluene** diisocyanate induced asthmatic reactions. A high correlation ($r = 0.97$; $p = 0.0006$) was obtained between the percent decrease in forced expiratory volume in 1 second during early asthmatic reactions and percent increase in neutrophil chemotactic activity. These observations support the hypothesis that activation of mast cells or basophils is associated with **toluene** diisocyanate induced early and late asthmatic reaction.
[Sastre J et al; J Allergy Clin Immunol 85 (3): 567-72 (1990)]**PEER REVIEWED**

In order to determine whether treatment with ketotifen inhibits asthmatic reactions induced by **toluene** di-isocyanate, six sensitized subjects with previously demonstrated dual or late asthmatic reaction after inhalation challenge with **toluene** diisocyanate were studied. Ketotifen (1 mg bid, orally) or placebo was administered for 7 days to the examined subjects, according to a double-blind, cross-over, placebo controlled study design. When the subjects were treated with either ketotifen or placebo, forced expiratory volume in 1 second markedly decr after exposure to **toluene** diisocyanate. These results suggest that the anti-asthmatic agent ketotifen is not effective in **toluene** diisocyanate induced asthma and suggest that it should not be used in the prophylaxis of asthmatic reactions induced by **toluene** diisocyanate in sensitized subjects.
[Tossin L et al; Clin Exp Allergy 19 (2): 177-82 (1989)]**PEER REVIEWED**

The beta-adrenoceptors on intact peripheral blood lymphocytes were studied in 21 allergic asthmatics, 11 **toluene** diisocyanate asthmatics and 17 normal subjects with radioligand binding assay technique. The airway responsiveness to methacholine provocation test was determined. The results indicated that beta-adrenoceptor Bmax values in allergic and **toluene** diisocyanate asthmatics were reduced but the affinity between receptor and ligand was increased; there was a positive correlation between the values

of Bmax and forced expiratory volume in 1 second%, V25/Pr in both asthmatic groups, a positive correlation between the values of Bmax and PC20 in allergic asthmatics. The beta-adrenoceptor responsiveness was remarkably reduced in allergic asthmatics.
[Yang ZF et al; Chin J Tuberc Respir Dis 12 (3): 143-146, 190-191. (1989)]**PEER REVIEWED**

Leukotriene B4 release from the lungs of sensitized subjects during asthmatic reactions induced by **toluene** diisocyanate was investigated. Three groups of **toluene** diisocyanate sensitized subjects were examined, one after no exposure to **toluene** diisocyanate, the second 8 hr after an exposure to **toluene** diisocyanate that caused an early asthmatic reaction, and the third 8 hr after an exposure to **toluene** diisocyanate that caused a late asthmatic reaction. Bronchoalveolar lavage fluid was analysed by reverse-phase HPLC and by specific radioimmunoassay. The mean concn of leukotriene B4 was higher (0.31 + or - 0.09 (standard error) ng/ml, range 0.15-0.51) in bronchoalveolar lavage fluid of sensitized subjects who developed a late asthmatic reaction than in bronchoalveolar lavage fluid of subjects who developed an early asthmatic reaction (0.05 + or - 0.04 ng/ml, range 0-0.224), and no leukotriene B4 was detectable in the control subjects. Bronchoalveolar lavage was also performed 8 hr after **toluene** diisocyanate exposure on four **toluene** diisocyanate sensitized late-dual reactors who were on steroid treatment. In this group of subjects no leukotriene B4 was detectable. These results suggest that leukotriene B4 may be involved in late asthmatic reactions induced by **toluene** diisocyanate.
[Zocca E et al; J Appl Physiol 68 (4): 576-80 (1990)]**PEER REVIEWED**

Interactions:

The effects of methacholine inhalation on airway responsiveness in **toluene** diisocyanate induced asthma were studied in six workers with a history of sensitivity to **toluene** diisocyanate. Symptoms among subjects included shortness of breath, wheezing, cough, and chest tightness at work, during the evening, or at night. A detailed cllnical and occupational history was taken for each subject, and lung function measurement and skin intradermal tests for common allergens were conducted. Airway responsiveness to methacholine was assessed before subjects were exposed for 30 minutes to 0.02 part per million **toluene** diisocyanate in an exposure chamber. Eight hours after **toluene** diisocyanate inhalation, airway responsiveness to methacholine was again determined. Forced expiratory volume was the measure of airway responsiveness. Although methacholine challenge was within normal limits when performed before **toluene** diisocyanate inhalation, the challenge went into the asthmatic range after **toluene** diisocyanate inhalation. Airway responsiveness increased significantly 8 hours after **toluene** diisocyanate challenge in the subjects and was accompanied by a decrease in forced expiratory volume. The late asthmatic reaction began between 3 and 5 hours asthma can be induced by **toluene** diisocyanate in the absence of airway responsiveness.
[Mapp CE et al; Eur J Respir Dis 68: 89-95 (1986)]**PEER REVIEWED**

Pharmacology:

Interactions:

The effects of methacholine inhalation on airway responsiveness in **toluene** diisocyanate induced asthma were studied in six workers with a history of sensitivity to **toluene** diisocyanate. Symptoms among subjects included shortness of breath, wheezing, cough, and chest tightness at work, during the evening, or at night. A detailed cllnical and occupational history was taken for each subject, and lung function

measurement and skin intradermal tests for common allergens were conducted. Airway responsiveness to methacholine was assessed before subjects were exposed for 30 minutes to 0.02 part per million **toluene** diisocyanate in an exposure chamber. Eight hours after **toluene** diisocyanate inhalation, airway responsiveness to methacholine was again determined. Forced expiratory volume was the measure of airway responsiveness. Although methacholine challenge was within normal limits when performed before **toluene** diisocyanate inhalation, the challenge went into the asthmatic range after **toluene** diisocyanate inhalation. Airway responsiveness increased significantly 8 hours after **toluene** diisocyanate challenge in the subjects and was accompanied by a decrease in forced expiratory volume. The late asthmatic reaction began between 3 and 5 hours asthma can be induced by **toluene** diisocyanate in the absence of airway responsiveness.
[Mapp CE et al; Eur J Respir Dis 68: 89-95 (1986)]**PEER REVIEWED**

Environmental Fate & Exposure:

Environmental Fate/Exposure Summary:

Commercial **toluene** diisocyanate (TDI) is composed of 2 isomers. 2,4-**Toluene** diisocyanate constitutes roughly 80% of TDI, the other 20% being the 2,6-isomer. It may be released to the environment as fugitive emissions and from stack exhaust during the production, transport, and use of TDI in the manufacture of polyurethane foam products and coatings as well as from spills. The types of reactions which the isomers undergo are similar, although the rates may differ. The reactivity of the 2,4-**toluene** diisocyanate with active hydrogen is greater than with the 2,6-isomer, therefore the percentage of 2,4-**toluene** diisocyanate in monitored TDI is generally much less than the 80% in the commercial mixture. However, since much of the monitoring data do not distinguish between isomers, it is not possible to know the proportion of the isomers in the TDI. If spilled on wet land, TDI is rapidly degraded. In one experiment simulating a spill, 5.5% of the original material remained after 24 hours and in a field situation, the concentration of TDI had declined to the ppm levels in 12 weeks. If released into water, a crust forms around the liquid TDI and <0.5% of the original material remains after 35 days. Low concentrations of TDI disappear from the aqueous environment in approximately a day. In the atmosphere, TDI reacts with photochemically produced hydroxyl radicals (half-life 3.3 hr) and is also removed by dry deposition. Human exposure is primarily occupational via inhalation and dermal contact. (SRC)
PEER REVIEWED

Probable Routes of Human Exposure:

Exposure to **toluene** diisocyanate is primarily occupational via inhalation or dermal contact with the aerosol or vapor. Workers may also be exposed through skin contact with freshly cured foam or as a result of spills or splashes. (SRC)
PEER REVIEWED

THE RESPIRATORY HEALTH OF 277 WORKERS IN A NEW **TOLUENE** DIISOCYANATE (TDI) MANUFACTURING PLANT WAS STUDIED PROSPECTIVELY DURING 5 YR OF EXPOSURE. PERSONAL TDI MONITORS WERE USED TO CONTINUOUSLY MEASURE PEAK & 8-HR TIME-WEIGHTED AVG (TWA) CONCN IN MORE THAN 2000 SAMPLES. REGRESSION OF ANNUAL CHANGE ON SMOKING (PACK-YEARS), ATOPIC STATUS & CUMULATIVE TDI EXPOSURE, DICHOTOMIZED AT 68.2 PPB MONTHS INTO LOW & HIGH EXPOSURE GROUPS,

SHOWED SIGNIFICANT EFFECTS OF SMOKING ON SPIROMETRIC TESTS & LUNG VOLUMES. AFTER ADJUSTING FOR PACK-YEARS OF SMOKING, THE 74 MEN IN THE HIGH CUMULATIVE TDI EXPOSURE CATEGORY HAD SIGNIFICANTLY LARGER DECLINE IN FEV1 (1-S FORCED EXPIRATORY VOLUME), % FEV (% FORCED EXPIRATORY VOLUME) & FEF25-75% (FORCED EXPIRATORY FRACTION FROM 25 TO 75% VITAL CAPACITY) THAN DID THE 149 MEN IN THE LOW CATEGORY. ANNUAL CHANGE IN FEV1 WAS THEN EXAMINED IN 6 SMOKING-EXPOSURE CATEGORIES: IN NEVER-SMOKERS, AVG ANNUAL DECLINE WAS 38 ML/YR GREATER IN THOSE WITH HIGHER CUMULATIVE TDI EXPOSURE.
[DIEM JE ET AL; AM REV RESPIR DIS 126 (3): 420 (1982)]**PEER REVIEWED**

VAPORS OF THESE COMPD INVARIABLY BECOME AIRBORNE IN POLYMERIZATION REACTIONS, ESP SINCE HEAT & GAS ARE EVOLVED. /**TOLUENE** DIISOCYANATES/
[Hamilton, A., and H. L. Hardy. Industrial Toxicology. 3rd ed. Acton, Mass.: Publishing Sciences Group, Inc., 1974. 335]**PEER REVIEWED**

NIOSH (NOHS Survey 1972-1974) has statistically estimated that 29,284 workers are exposed to TDI in the USA(1). NIOSH (NOES Survey 1981-1983) has statistically estimated that 6,044 workers are exposed to TDI in the USA(2). Since the NOES survey excludes exposure to trade name chemicals which may contain the chemical, occupational exposure could be considerably higher(SRC).
[(1) NIOSH; National Occupational Health Survey (1974) (2) NIOSH; National Occupational Exposure Survey (1983)]**PEER REVIEWED**

Concentration medians for 2,4-**toluene** diisocyanate in 2 plants producing flexible polyurethane foam were 0.70 and 0.33 ppb for the mixing and finishing ends, respectively(1). The respective median values for 2,6-TDI were 0.91 and 1.1 ppb. Maximum concentrations of 2,6-TDI exceeded 64 ppb at the finishing end(1).
[(1) Rando RJ et al; Am Ind Hyg Assoc J 45: 199-203 (1984)]**PEER REVIEWED**

In a Finnish study, TDI vapor concentrations ranged from 25-80 ug/cu m for pouring, 14-44 ug/cu m for paper stripping, and 1-8 ug/cu m for cutting(1). Personal monitors measured 9-34 ug/cu m and 5-30 ug/cu m of the 2,4-isomer for pouring and paper stripping, respectively(1). While 2,4-**toluene** diisocyanate constitutes 80% of TDI, and 2,6-**toluene** diisocyanate 20%, the 2,4-isomer is more reactive so that the concentration of the 2,6-isomer is higher in workplace air(1). The percentage of 2,4-**toluene** diisocyanate to total **toluene** diisocyanate measured with the personal monitors ranged from 29 to 69%(1). TDI levels of 1.3-2.8 ppb were detected in air inside a Swedish factory manufacturing polyurethanes(2).
[(1) Rosenberg C, Savolainen H; J Chromatography 367: 385-92 (1986) (2) Audunsson G et al; Intern J Environ Anal Chem 20: 85-100 (1985)]**PEER REVIEWED**

Mean concn ranges of TDI reported in ambient workplace air were 0.7-710 ug/cu m in TDI production, ND - 1490 ug/cu m during polyurethane foam production, 70-140 mg/cu m during elastomer production, 13 - 1050 ug/cu m during polyurethane foam use, 10-710 ug/cu m during polyurethane spray paint use, and <1-740 ug/cu m during the production of polyurethane-coated wire(1). Mean concn in personal

samples ranged from ND-540 ug/cu m during polyurethane foam production and 2-1220 ug/cu m during polyurethane spray foam use(1). Additionally, mean concn of TDI released from insulation in a ship's hold was reported to be 120-150 ug/cu m and that released from coated fabric in a workplace 2-10 ug/cu m(1). During the outdoor application of TDI foam to a 40 ft diameter storage tanks, the mean atmospheric TDI concentration downwind from the spray gun was 0.3 ppm at 8 ft, 0.02 ppm at 40 ft, and 0.002 ppm at 150 ft(2). TDI was not detected more than 8 ft upwind of the spray gun(2). Air samples taken within two ft of the foam surface immediately after spraying had ceased was found to be 0.03 ppm(2). Mean TDI concentrations near the pumping equipment during material transfer was 0.02 ppm(2).
[(1) IARC Monograph on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. 39: 287-323 (1985) (2) Peterson JE et al; Amer Id Hyg Assoc J 23: 345-52 (1962)]**PEER REVIEWED**

Natural Pollution Sources:

2,4- and 2,6-**toluene** diisocyanate, the components of commercial TDI are not known to occur as a natural product(1).
[(1) IARC; Monograph on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. 19: 303-11 (1979)]**PEER REVIEWED**

Artificial Pollution Sources:

Levels of 100-17,700 ug/cu m **toluene** diisocyanate were reported in samples from the stack exhaust of a polyurethane foam production plant.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 299 (1986)]**PEER REVIEWED**

TDI may be released to the environment, primarily as stack and fugitive emissions into air during its commercial production, handling, and processing prior to polyurethane foam production(1). It may also be released during the manufacture of polyurethane foam products and coatings, from sprays, insulation materials, and polyurethane foam coated fabrics(1,3). About 0.005% of the TDI used in flexible foam slabstock plants is released in vent stack exhaust and this contains <50% of the 2,4-isomer(2). Large quantities of TDI are transported by rail, road, and sea and releases may occur from accidental spills on land or in surface waters during loading or transit(2).
[(1) IARC Monograph on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. 39: 287-323 (1985) (2) Brochhagen FK, Grieveson BM; Cellular Polymers 3: 11-7 (1984) (3) Duff PB; pp. 408-12 in Polyurethane-New Paths to Progress Marketing Technology Proc of the SPI 6th Inter Tech/Market Conf (1983)]**PEER REVIEWED**

Environmental Fate:

TERRESTRIAL FATE: Ten days after a spill of 13 tons of **toluene** diisocyanate (TDI) onto swampy, wet forest soil, TDI and toluenediamines were found in the soil(1,2). The TDI solidified and the area was covered with sand. The soil concn of TDI and toluenediamine combined declined from the parts per thousand to parts per million range between 10 days and 12 wk after the spill(2). No TDI was detected in

a connecting brook 10 days after the spill(2). After 6 years only TDI-derived polyureas were found at the site(1). In a simulated spill, 5 kg of TDI in a container was covered with 50 kg of sand and 5 kg of water at ambient temperatures and samples taken from the top and bottom of the sand pile. After 24 hr, 5.5% of the TDI remained unreacted and after 8 days 3.5% remained(2). The reaction product was largely polyureas(2).
[(1) IARC Monograph on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. 39: 287-323 (1985) (2) Brochhagen FK, Grieveson BM; Cellular Ploymers 3: 11-7 (1984)]**PEER REVIEWED**

AQUATIC FATE: When low concns of TDI are released into model river or seaway systems, it is hydrolyzed within a day. In order to simulate a spill of TDI in stagnant water, 0.5 liters of TDI was poured into 20 liters of water of pH 5, 7, or 9 at 20 deg C. A hard compact crust formed at the water TDI interface(1). This crust thickened over a period of 30 days until no liquid TDI remained. The solid crust contained <0.5% of the original TDI after 35 days(1). Another experiment were performed to simulate a spill into running water by pouring 0.5 l of TDI into 20 l of slowly overflowing water. Barely detectable amounts of toluenediamine were present in the overflow samples. As in the stagant water simulation, a crust formed that contained <0.5% of the original TDI after 35 days(1).
[(1) Brochhagen FK, Grieveson BM; Cellular Ploymers 3: 11-17 (1984)]**PEER REVIEWED**

ATMOSPHERIC FATE: Removal of TDI from the atmosphere is due to reaction with photochemically produced hydroxyl radicals (half-life 3.3 hr) as well as through dry deposition. Earlier ideas that reaction with water vapor was of major importance have not been substantiated in recent experiments.(SRC)
PEER REVIEWED

Environmental Biodegradation:

Toluene diisocyanates are expected to be hydrolyzed much more rapidly than they are attacked by microorganisms. The resulting **toluene** diamines are subject to a wide variety of biochemical transformations.
[ITC/USEPA; Information Review #231 (Draft) Toluene Diisocyanates p. 19 (1981)]**PEER REVIEWED**

Environmental Abiotic Degradation:

Toluene diisocyanate reacts readily with compounds containing active hydrogens, such as water, acids, and alcohols(2). Contact with bases may cause uncontrollable polymerization with rapid evolution of heat(2). In concentrated solutions, hydrolysis of one of the isocyanate groups to the amine is followed by rapid reaction of the amine with an isocyanate group on another molecule leading to dimers, oligimers, and polymers(2). In one experiment the hydrolysis product yield was 20% diamine and 80% polyurea(3). When 50 ppm of **toluene** diisocyanate was added to model river and seawater systems, the concn fell to 0.1 ppm or less at the end of 1 day(1).
[(1) Duff PB; The Fate of TDI in the Environment. In: Polyurethane-New Paths to Progress Marketing Technology. Proc. of the SPI 6th Inter. Tech. Marketing Conf. pp. 408-12 (1983) (2) IARC Monograph on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. 39: 287-323 (1985) (3) Sopach ED, Boltromeyuk LP; Gig Sanit 7: 10-3 (1974)]**PEER REVIEWED**

Gas phase loss of TDI was originally thought to be due to reaction of TDI with water vapor. One early work showed that the percent disappearance of TDI in air depended almost solely on the water vapor concentration, increasing 3.2% per unit increase in absolute humidity (g water/kg dry air), so that at 15 g water/kg dry air, a 50% reduction in TDI was obtained(2). These reductions were obtained after 8 sec and did not differ appreciably after 75 sec(2). More recent work contradicted these earlier findings and a program was instituted to study the gas-phase reactions between TDI and water using a room sized environmental chamber(1). They found that over a relative humidity range of 7-70%, the loss rate of TDI was independent of humidity and no toluenediamine or TDI-urea products could be detected(1). No evidence of gas phase reaction between water and TDI could be detected. The loss of TDI was due to adsorption to the chamber walls(1).
[(1) Holdren MW et al; Am Ind Hyg Assoc J 45: 626-33 (1984) (2) Dyson WL, Hermann ER; Amer Ind Hyg Assoc J 32: 741-4 (1971)]**PEER REVIEWED**

Subsequent experiments were performed in the environmental chamber to assess the importance of photolysis, reaction with free radicals, and adsorption onto particulate matter as atmospheric removal processes(1). The loss rate of TDI in irradiated clean air was first order with a half-life of 3.3 hr(1). By using a free radical scavenger, it was shown that free-radicals and not photolysis was responsible for the removal. The half-life is consistant with the reaction with photochemically generated hydroxyl radicals(1). The addition of a urban surrogate hydrocarbon mixture (polluted urban air), did not significantly alter removal rates(1). The concentration of hydroxyl radicals generally increases in polluted air resulting in shorter half-lives which were not observed in the above study(SRC). Adsorption to particulate matter was not significant(1).
[(1) Duff PB; Proc of the SPI Tech/Mark Conf 29: 9-14 (1985)]**PEER REVIEWED**

Volatilization from Water/Soil:

The vapor pressure of TDI is 0.01 torr at 20 deg C(1), and therefore spilled TDI will not readily volatilize from soil surfaces or other surfaces(SRC). Since TDI reacts with water, volatilization from water should not be important(SRC).
[(1) IARC Monograph on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. 39: 287-323 (1985)]**PEER REVIEWED**

Environmental Water Concentrations:

Toluene diisocyanate has been reported in the waste-water of a furniture manufacturing area in a concn range of 0.1-4.1 mg/l.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 299 (1986)]**PEER REVIEWED**

Effluent Concentrations:

TDI has been reported in waste water from furniture manufacturing in the concn range of 0.1-4.1 ppm(1). However the coloremetric method used did not distinguish between the disocyanate or the corresponding amine(1). In view of TDI's rapid reactivity with water, it is probable that the chemical detected was the

corresponding amine(SRC). Stack exhaust from a polyurethane foam production plant were reported to contain 100-17,700 ug/cu m of TDI(1).
[(1) IARC Monograph on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. 39: 287-323 (1985)]**PEER REVIEWED**

Sediment/Soil Concentrations:

Ten days after an accident resulting in the spillage of 13 tons of **toluene** diisocyanate from a lorry on a swampy wet forest area, **toluene** diisocyanate and toluenediamine were /found/ in the soil. After six yr, only **toluene** diisocyanate-derived polyureas were found in soil samples taken at the same site.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 299 (1986)]**PEER REVIEWED**

Other Environmental Concentrations:

TDI monomer has been found in a urethane foam fabric coating in concn of <200 ppm(1).
[(1) IARC Monograph on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. 39: 287-323 (1985)]**PEER REVIEWED**

Environmental Standards & Regulations:

TSCA Requirements:

Pursuant to section 8(d) of TSCA, EPA promulgated a model Health and Safety Data Reporting Rule. The section 8(d) model rule requires manufacturers, importers, and processors of listed chemical substances and mixtures to submit to EPA copies and lists of unpublished health and safety studies. Benzene, 1,3-diisocyanatomethyl- is included on this list.
[40 CFR 716.120 (7/1/91)]**PEER REVIEWED**

CERCLA Reportable Quantities:

Persons in charge of vessels or facilities are required to notify the National Response Center (NRC) immediately, when there is a release of this designated hazardous substance, in an amount equal to or greater than its reportable quantity of 100 lb or 45.4 kg. The toll free number of the NRC is (800) 424-8802; In the Washington D.C. metropolitan area (202) 426-2675. The rule for determining when notification is required is stated in 40 CFR 302.4 (section IV. D.3.b).
[40 CFR 302.4 (7/1/91)]**PEER REVIEWED**

RCRA Requirements:

U223; As stipulated in 40 CFR 261.33, when **toluene** diisocyanate, as a commercial chemical product or manufacturing chemical intermediate or an off-specification commercial chemical product or a manufacturing chemical intermediate, becomes a waste, it must be managed according to Federal and/or State hazardous waste regulations. Also defined as a hazardous waste is any residue, contaminated soil, water, or other debris resulting from the cleanup of a spill, into water or on dry land, of this waste. Generators of small quantities of this waste may qualify for partial exclusion from hazardous waste regulations (40 CFR 261.5).

[40 CFR 261.33 (7/1/91)]**PEER REVIEWED**

Atmospheric Standards:

This action promulgates standards of performance for equipment leaks of Volatile Organic Compounds (VOC) in the Synthetic Organic Chemical Manufacturing Industry (SOCMI). The intended effect of these standards is to require all newly constructed, modified, and reconstructed SOCMI process units to use the best demonstrated system of continuous emission reduction for equipment leaks of VOC, considering costs, non air quality health and environmental impact and energy requirements. **Toluene** diisocyanate is produced, as an intermediate or a final product, by process units covered under this subpart.
[40 CFR 60.489 (7/1/91)]**PEER REVIEWED**

Chemical/Physical Properties:

Molecular Formula:

C9-H6-N2-O2
PEER REVIEWED

Color/Form:

Clear colorless to pale yellow liquid.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, D.C.: Assoc. of American Railroads,Hazardous Materials Systems (BOE), 1987. 686]**PEER REVIEWED**

Odor:

Pungent odor
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, D.C.: Assoc. of American Railroads,Hazardous Materials Systems (BOE), 1987. 686]**PEER REVIEWED**

Boiling Point:

251 deg C
[ITC/USEPA; Information Review #231 (Draft) Toluene Diisocyanates p.2 (1981)]**PEER REVIEWED**

Melting Point:

11-14 deg C (freezing point)
[Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984.,p. V15 790 (1981)]**PEER REVIEWED**

Density/Specific Gravity:

1.22 + or - 0.01 g/ml at 25 deg C
[ITC/USEPA; Information Review #231 (Draft) Toluene Diisocyanates p.2 (1981)]**PEER REVIEWED**

Spectral Properties:

Refractive Index 1.5666 at 25 deg C (80:20 mix); 1.5663 at 25 deg C (65:35 mixture)
[Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984.,p. V15 790 (1981)]**PEER REVIEWED**

Vapor Pressure:

0.01 torr at 20 deg C
[IARC Monograph on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. 39: 287-323 (1985)]**PEER REVIEWED**

Other Chemical/Physical Properties:

VAPOR PRESSURE: 0.5 MM @ 25 DEG C /80% 2,4:20% 2,6/
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values, 4th ed., 1980. Cincinnati, Ohio: American Conference ofGovernmmental Industrial Hygienists, Inc., 1980. 401]**PEER REVIEWED**

MISCIBLE WITH ALCOHOL, ETHER, ACETONE /80% 2,4:20% 2,6/
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values, 4th ed., 1980. Cincinnati, Ohio: American Conference ofGovernmmental Industrial Hygienists, Inc., 1980. 401]**PEER REVIEWED**

MISCIBLE WITH CARBON TETRACHLORIDE /80% 2,4:20% 2,6/
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values, 4th ed., 1980. Cincinnati, Ohio: American Conference ofGovernmmental Industrial Hygienists, Inc., 1980. 401]**PEER REVIEWED**

MISCIBLE WITH BENZENE, KEROSENE /80% 2,4:20% 2,6/
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values, 4th ed., 1980. Cincinnati, Ohio: American Conference ofGovernmmental Industrial Hygienists, Inc., 1980. 401]**PEER REVIEWED**

SPECIFIC GRAVITY: 1.22 @ 25 DEG C; BP: 250 DEG C; FP: 11.3-13.5 DEG C /80% 2,4:20% 2,6/
[American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices. 5th ed. Cincinnati, OH:American Conference of Governmental Industrial Hygienists, 1986. 580]**PEER REVIEWED**

Chemical Safety & Handling:

DOT Emergency Guidelines:

Fire or explosion: Combustible material: may burn but does not ignite readily. Substance will react with water (some violently) releasing flammable, toxic or corrosive gases and runoff. When heated, vapors may form explosive mixtures with air: indoors, outdoors, and sewers explosion hazards. Most vapors are heavier than air. They will spread along ground and collect in low or confined areas (sewers, basements, tanks). Vapors may travel to source of ignition and flash back. Contact with metals may evolve flammable hydrogen gas. Containers may explode when heated or if contaminated with water.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-156]**QC REVIEWED**

Health: TOXIC; inhalation, ingestion or contact (skin, eyes) with vapors, dusts or substance may cause severe injury, burns, or death. Reaction with water or moist air will release toxic, corrosive or flammable gases. Reaction with water may generate much heat which will increase the concentration of fumes in the air. Fire will produce irritating, corrosive and/or toxic gases. Runoff from fire control or dilution water may be corrosive and/or toxic and cause pollution.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-156]**QC REVIEWED**

Public safety: CALL Emergency Response Telephone Number on Shipping Paper first. If Shipping Paper not available or no answer, refer to appropriate telephone number listed on the inside back cover. Isolate spill or leak area immediately for at least 50 to 100 meters (160 to 330 feet) in all directions. Keep unauthorized personnel away. Stay upwind. Keep out of low areas. Ventilate enclosed areas.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-156]**QC REVIEWED**

Protective clothing: Wear positive pressure self-contained breathing apparatus (SCBA). Wear chemical protective clothing which is specifically recommended by the manufacturer. Structural firefighters' protective clothing is recommended for fire situations ONLY; it is not effective in spill situations.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs

Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-156]**QC REVIEWED**

Evacuation: Spill: See the Table of Initial Isolation and Protective Action Distances for highlighted substances. For non-highlighted substances, increase, in the downwind direction, as necessary, the isolation distance shown under "PUBLIC SAFETY". Fire: If tank, rail car or tank truck is involved in a fire, ISOLATE for 800 meters (1/2 mile) in all directions; also, consider initial evacuation for 800 meters (1/2 mile) in all directions.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-156]**QC REVIEWED**

Fire: Note: Most foams will react with the material and release corrosive/toxic gases. Small fires: CO2, dry chemical, dry sand, alcohol-resistant foam. Large fires: Water spray, fog or alcohol-resistant foam. FOR CHLOROSILANES, DO NOT USE WATER; use AFFF alcohol-resistant medium expansion foam. Move containers from fire area if you can do it without risk. Do not use straight streams. Fire involving tanks or car/trailer loads: Fight fire from maximum distance or use unmanned hose holders or monitor nozzles. Do not get water inside containers. Cool containers with flooding quantities of water until well after fire is out. Withdraw immediately in case of rising sound from venting safety devices or discoloration of tank. ALWAYS stay away from the ends of tanks.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-156]**QC REVIEWED**

Spill or leak: ELIMINATE all ignition sources (no smoking, flares, sparks or flames in immediate area). All equipment used when handling the product must be grounded. Do not touch damaged containers or spilled material unless wearing appropriate protective clothing. Stop leak if you can do it without risk. A vapor suppressing foam may be used to reduce vapors. FOR CHLOROSILANES, use AFFF alcohol-resistant medium expansion foam to reduce vapors. DO NOT GET WATER on spilled substance or inside containers. Use water spray to reduce vapors or divert vapor cloud drift. Prevent entry into waterways, sewers, basements or confined areas. Small spills: Cover with DRY earth, DRY sand, or other non-combustible material followed with plastic sheet to minimize spreading or contact with rain. Use clean non-sparking tools to collect material and place it into loosely covered plastic containers for later disposal.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-156]**QC REVIEWED**

First aid: Move victim to fresh air. Call emergency medical care. Apply artificial respiration if victim is not breathing. Do not use mouth-to-mouth method if victim ingested or inhaled the substance; induce artificial respiration with the aid of a pocket mask equipped with a one-way valve or other proper respiratory medical device. Administer oxygen if breathing is difficult. Remove and isolate contaminated clothing and shoes. In case of contact with substance, immediately flush skin or eyes with running water for at least 20 minutes. For minor skin contact, avoid spreading material on unaffected skin. Keep victim warm and quiet. Effects of exposure (inhalation, ingestion or skin contact) to substance may be delayed. Ensure that medical personnel are aware of the material(s) involved, and take precautions to protect themselves.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-156]**QC REVIEWED**

Odor Threshold:

Odor recognition in air: 2.10 ppm (purity)
[Fazzalari, F.A. (ed.). Compilation of Odor and Taste Threshold Values Data. ASTM Data Series DS 48A (Committee E-18). Philadelphia, PA: American Society for Testing and Materials, 1978. 158]**PEER REVIEWED**

TOLUENE DIISOCYANATE HAS MARKED CHARACTERISTIC ODOR WHICH ALLOWS IT TO BE DETECTED READILY. YET @ MAX RECOMMENDED CONCN (0.02 PPM) THE POISON CANNOT BE DETECTED BY ITS SMELL.
[Lefaux, R. Practical Toxicology of Plastics. Cleveland: CRC Press Inc., 1968. 102]**PEER REVIEWED**

Skin, Eye and Respiratory Irritations:

AS A VAPOR ... /**TOLUENE** DIISOCYANATE/ IS A POWERFUL IRRITANT TO EYES, SKIN, RESPIRATORY TRACT.
[Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984.,p. II-414]**PEER REVIEWED**

Fire Potential:

DUE TO ITS HIGH FLASH POINT, **TOLUENE** DIISOCYANATE OFFERS NO SERIOUS RISK OF FIRE ... .
[Lefaux, R. Practical Toxicology of Plastics. Cleveland: CRC Press Inc., 1968. 103]**PEER REVIEWED**

Combustible when exposed to heat or flame.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39

288 (1986)]**PEER REVIEWED**

Flash Point:

270 DEG F CLOSED CUP /80% 2,4:20% 2,6/
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values, 4th ed., 1980. Cincinnati, Ohio: American Conference ofGovernmmental Industrial Hygienists, Inc., 1980. 401]**PEER REVIEWED**

132 deg C (open cup)
[Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984.,p. V15 791 (1981)]**PEER REVIEWED**

Fire Fighting Procedures:

FIREFIGHTERS MUST BE PROTECTED AGAINST DIISOCYANATE VAPORS & NO2 BY COMPLETE PROTECTIVE EQUIPMENT (CLOSED-CIRCUIT BREATHING APPARATUS, RUBBER GLOVES, ETC). /DIISOCYANATES/
[Lefaux, R. Practical Toxicology of Plastics. Cleveland: CRC Press Inc., 1968. 103]**PEER REVIEWED**

Firemen must be equipped with self-contained breathing apparatus. /Isocyanates/
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 1162]**PEER REVIEWED**

If material on fire or involved in fire: Do not extinguish fire unless flow can be stopped. Use water in flooding quantities as fog. Solid streams of water may be ineffective. Cool all affected containers with flooding quantities of water. Apply water from as far a distance as possible. Use "alcohol" foam, carbon dioxide, or dry chemical. Use water spray to knock-down vapors.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, D.C.: Assoc. of American Railroads,Hazardous Materials Systems (BOE), 1987. 686]**PEER REVIEWED**

Toxic Combustion Products:

Toxic oxides of nitrogen are produced during combustion of this material.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, D.C.: Assoc. of American Railroads,Hazardous Materials Systems (BOE), 1987. 686]**PEER REVIEWED**

Hazardous Reactivities & Incompatibilities:

It can react with aniline. The heat of this reaction may be sufficient to ignite surrounding combustibles and the material itself.
[Association of American Railroads. Emergency Handling of Hazardous

Materials in Surface Transportation. Washington, D.C.: Assoc. of American Railroads,Hazardous Materials Systems (BOE), 1987. 686]**PEER REVIEWED**

Strong oxidizers, water, acids, bases and amines (may cause foam and splatter); alcohols. [Note: Reacts slowly with water to form carbon dioxide and polyureas.] /**Toluene** 2,4-diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

Hazardous Decomposition:

... WHEN HEATED TO DECOMPOSITION, IT EMITS HIGHLY TOXIC FUMES OF /HYDROGEN CHLORIDE AND NITROGEN OXIDES/.
[Sax, N.I. Dangerous Properties of Industrial Materials. 6th ed. New York, NY: Van Nostrand Reinhold, 1984. 2590]**PEER REVIEWED**

Immediately Dangerous to Life or Health:

NIOSH considers 2,4-**toluene** diisocyanate to be a potential occupational carcinogen. /2,4-**Toluene** diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

Protective Equipment & Clothing:

... Provide the workers with protective clothing, gloves and goggles. Respiratory protection may be provided by masks incorporating a prefilter, but the best form of protection in work carried on in a high concn of isocyanates is air-supplied breathing apparatus. /Isocyanates/
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 1162]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": ... dispensers of liq detergent /should be available./ ... Safety pipettes should be used for all pipetting. ... In animal laboratory, personnel should ... wear protective suits (preferably disposable, one-piece & close-fitting at ankles & wrists), gloves, hair covering & overshoes. ... In chemical laboratory, gloves & gowns should always be worn ... however, gloves should not be assumed to provide full protection. Carefully fitted masks or respirators may be necessary when working with particulates or gases, & disposable plastic aprons might provide addnl protection. ... Gowns ... /should be/ of distinctive color, this is a reminder that they are not to be worn outside the laboratory. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 8]**PEER REVIEWED**

Three commercial air-purifying respirators for protection against **toluene** diisocyanate vapors were

evaluated. The Willson R-21 and Survivair, organic vapor cartridges, and the disposable, valveless 3M-8711 were the three respirators evaluated. Each respirator/cartridge was tested three times at 0.2 ppm **toluene** diisocyanate concn for 40 hr and once for 20 hr or more at concn greater than 1.5 ppm **toluene** diisocyanate. All cartridges/respirators had the capacity to provide the required protection against **toluene** diisocyanate vapors. Additional considerations in the respirator selection process included the training and experience of the respirator user, the enforcement of the respirator program, fit of the respirator, knowledge of **toluene** diisocyanate concn onsite, presence of other solvents or chemicals in the air which may adversely affect the capacity of the respirato for **toluene** diisocyanate, and the high odor threshold of **toluene** diisocyanate that makes it impossible for the user to receive advance warning of a leak.
[Dharmarajan V et al; Am Ind Hyg Assoc 47 (7): 393-8 (1986)]**PEER REVIEWED**

Wear appropriate eye protection to prevent eye contact. /**Toluene** 2,4-diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

Wear appropriate personal protective clothing to prevent skin contact. /**Toluene** 2,4-diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

Eyewash fountains should be provided in areas where there is any possibility that workers could be exposed to the substance; this is irrespective of the recommendation involving the wearing of eye protection. /**Toluene** 2,4-diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

Facilities for quickly drenching the body should be provided within the immediate work area for emergency use where there is a possibility of exposure. (Note: It is intended that these facilities provide a sufficient quantity or flow of water to quickly remove the substance from any body areas likely to be exposed. The actual determination of what constitutes an adequate quick drench facility depends on the specific circumstances. In certain instances, a deluge shower should be readily available, whereas in others, the availability of water from a sink or hose could be considered adequate.) /**Toluene** 2,4-diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

Recommendations for respirator selection: Condition: At concentrations above the NIOSH REL, or where there is no REL, at any detectable concentration: Respirator Class(es): Any self-contained breathing apparatus that has a full facepiece and is operated in a pressure-demand or other positive pressure-mode. Any supplied-air respirator that has a full facepiece and is operated in a pressure-demand or other positive-pressure mode in combination with an auxiliary self-contained breathing apparatus operated in pressure-demand or other positive-pressure mode. /**Toluene** 2,4-diisocyanate/

[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

Recommendations for respirator selection: Escape from suddenly occurring respiratory hazards: Respirator Class(es): Any air-purifying, full-facepiece respirator (gas mask) with a chin-style, front- or back-mounted organic vapor canister. Any appropriate escape-type, self-contained breathing apparatus. /**Toluene** 2,4-diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

Preventive Measures:

VENTILATION SHOULD BE ADEQUATE ... OUTDOOR SPRAYING OPERATIONS SHOULD BE SHIELDED ... IF POLYURETHANE PRODUCTS ARE HEATED ... PROTECTION AGAINST ISOCYANATES THUS RELEASED IS NECESSARY. /ISOCYANATES/
[International Labour Office. Encyclopedia of Occupational Health and Safety. Volumes I and II. New York: McGraw-Hill Book Co., 1971. 746]**PEER REVIEWED**

The sanitary facilities ... /for/ workers must incl showers. /Isocyanates/
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 1162]**PEER REVIEWED**

If material not on fire and not involved in fire: Keep sparks, flames, and other sources of ignition away. Keep material out of water sources and sewers. Build dikes to contain flow as necessary. Attempt to stop leak if without hazard. Use water spray to knock-down vapors.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, D.C.: Assoc. of American Railroads,Hazardous Materials Systems (BOE), 1987. 686]**PEER REVIEWED**

Personnel protection: Avoid breathing vapors. Keep upwind. Avoid bodily contact with the material. Do not handle broken packages without protective equipment. Wash away any material which may have contacted the body with copious amounts of water or soap and water.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, D.C.: Assoc. of American Railroads,Hazardous Materials Systems (BOE), 1987. 686]**PEER REVIEWED**

Evacuation: If material leaking (not on fire), consider evacuation from downwind area based on amount of material spilled, location and weather conditions.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, D.C.: Assoc. of American Railroads,Hazardous Materials Systems (BOE), 1987. 686]**PEER REVIEWED**

SRP: Contaminated protective clothing should be segregated in such a manner so that there is no direct personal contact by personnel who handle, dispose, or clean the clothing. Quality assurance to ascertain the completeness of the cleaning procedures should be implemented before the decontaminated protective clothing is returned for reuse by the workers. Contaminated clothing should not be taken home at end of shift, but should remain at employee's place of work for cleaning.
PEER REVIEWED

PRECAUTIONS FOR "CARCINOGENS": Smoking, drinking, eating, storage of food or of food & beverage containers or utensils, & the application of cosmetics should be prohibited in any laboratory. All personnel should remove gloves, if worn, after completion of procedures in which carcinogens have been used. They should ... wash ... hands, preferably using dispensers of liq detergent, & rinse ... thoroughly. Consideration should be given to appropriate methods for cleaning the skin, depending on nature of the contaminant. No standard procedure can be recommended, but the use of organic solvents should be avoided. Safety pipettes should be used for all pipetting. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 8]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": In animal laboratory, personnel should remove their outdoor clothes & wear protective suits (preferably disposable, one-piece & close-fitting at ankles & wrists), gloves, hair covering & overshoes. ... Clothing should be changed daily but ... discarded immediately if obvious contamination occurs ... /also,/ workers should shower immediately. In chemical laboratory, gloves & gowns should always be worn ... however, gloves should not be assumed to provide full protection. Carefully fitted masks or respirators may be necessary when working with particulates or gases, & disposable plastic aprons might provide addnl protection. If gowns are of distinctive color, this is a reminder that they should not be worn outside of lab. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 8]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": ... Operations connected with synth & purification ... should be carried out under well-ventilated hood. Analytical procedures ... should be carried out with care & vapors evolved during ... procedures should be removed. ... Expert advice should be obtained before existing fume cupboards are used ... & when new fume cupboards are installed. It is desirable that there be means for decreasing the rate of air extraction, so that carcinogenic powders can be handled without ... powder being blown around the hood. Glove boxes should be kept under negative air pressure. Air changes should be adequate, so that concn of vapors of volatile carcinogens will not occur. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 8]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": Vertical laminar-flow biological safety cabinets may be used for containment of in vitro procedures ... provided that the exhaust air flow is sufficient to provide an inward air flow at the face opening of the cabinet, & contaminated air plenums that are under positive pressure are leak-tight. Horizontal laminar-flow hoods or safety cabinets, where filtered air is blown across the working area towards the operator, should never be used ... Each cabinet or fume cupboard to be used ... should be tested before work is begun (eg, with fume bomb) & label fixed to it, giving date of test & avg air-flow measured. This test should be repeated periodically & after any structural changes. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 9]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": Principles that apply to chem or biochem lab also apply to microbiological & cell-culture labs ... Special consideration should be given to route of admin. ... Safest method of administering volatile carcinogen is by injection of a soln. Admin by topical application, gavage, or intratracheal instillation should be performed under hood. If chem will be exhaled, animals should be kept under hood during this period. Inhalation exposure requires special equipment. ... unless specifically required, routes of admin other than in the diet should be used. Mixing of carcinogen in diet should be carried out in sealed mixers under fume hood, from which the exhaust is fitted with an efficient particulate filter. Techniques for cleaning mixer & hood should be devised before expt begun. When mixing diets, special protective clothing &, possibly, respirators may be required. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 9]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": When ... admin in diet or applied to skin, animals should be kept in cages with solid bottoms & sides & fitted with a filter top. When volatile carcinogens are given, filter tops should not be used. Cages which have been used to house animals that received carcinogens should be decontaminated. Cage-cleaning facilities should be installed in area in which carcinogens are being used, to avoid moving of ... contaminated /cages/. It is difficult to ensure that cages are decontaminated, & monitoring methods are necessary. Situations may exist in which the use of disposable cages should be recommended, depending on type & amt of carcinogen & efficiency with which it can be removed. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 10]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": To eliminate risk that ... contamination in lab could build up during conduct of expt, periodic checks should be carried out on lab atmospheres, surfaces, such as walls, floors & benches, & ... interior of fume hoods & airducts. As well as regular monitoring, check must be

carried out after cleaning-up of spillage. Sensitive methods are required when testing lab atmospheres. ... Methods ... should ... where possible, be simple & sensitive. ... /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 10]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": Rooms in which obvious contamination has occurred, such as spillage, should be decontaminated by lab personnel engaged in expt. Design of expt should ... avoid contamination of permanent equipment. ... Procedures should ensure that maintenance workers are not exposed to carcinogens. ... Particular care should be taken to avoid contamination of drains or ventilation ducts. In cleaning labs, procedures should be used which do not produce aerosols or dispersal of dust, ie, wet mop or vacuum cleaner equipped with high-efficiency particulate filter on exhaust, which are avail commercially, should be used. Sweeping, brushing & use of dry dusters or mops should be prohibited. Grossly contaminated cleaning materials should not be re-used ... If gowns or towels are contaminated, they should not be sent to laundry, but ... decontaminated or burnt, to avoid any hazard to laundry personnel. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 10]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": Doors leading into areas where carcinogens are used ... should be marked distinctively with appropriate labels. Access ... limited to persons involved in expt. ... A prominently displayed notice should give the name of the Scientific Investigator or other person who can advise in an emergency & who can inform others (such as firemen) on the handling of carcinogenic substances. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 11]**PEER REVIEWED**

SRP: The scientific literature for the use of contact lenses in industry is conflicting. The benefit or detrimental effects of wearing contact lenses depend not only upon the substance, but also on factors including the form of the substance, characteristics and duration of the exposure, the uses of other eye protection equipment, and the hygiene of the lenses. However, there may be individual substances whose irritating or corrosive properties are such that the wearing of contact lenses would be harmful to the eye. In those specific cases, contact lenses should not be worn. In any event, the usual eye protection equipment should be worn even when contact lenses are in place.
QC REVIEWED

The worker should immediately wash the skin when it becomes contaminated. /**Toluene** 2,4-diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH)

Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

The worker should wash daily at the end of each work shift. /**Toluene** 2,4-diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

Work clothing that becomes wet or significantly contaminated should be removed and replaced. /**Toluene** 2,4-diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

Workers whose clothing may have become contaminated should change into uncontaminated clothing before leaving the work premises. /**Toluene** 2,4-diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

Shipment Methods and Regulations:

No person may /transport,/ offer or accept a hazardous material for transportation in commerce unless that person is registered in conformance ... and the hazardous material is properly classed, described, packaged, marked, labeled, and in condition for shipment as required or authorized by ... /the hazardous materials regulations (49 CFR 171-177)./
[49 CFR 171.2 (7/1/96)]**QC REVIEWED**

The International Air Transport Association (IATA) Dangerous Goods Regulations are published by the IATA Dangerous Goods Board pursuant to IATA Resolutions 618 and 619 and constitute a manual of industry carrier regulations to be followed by all IATA Member airlines when transporting hazardous materials.
[IATA. Dangerous Goods Regulations. 38th ed. Montreal, Canada and Geneva, Switzerland: International Air Transport Association, Dangerous Goods Board, January, 1997. 221]**QC REVIEWED**

The International Maritime Dangerous Goods Code lays down basic principles for transporting hazardous chemicals. Detailed recommendations for individual substances and a number of recommendations for good practice are included in the classes dealing with such substances. A general index of technical names has also been compiled. This index should always be consulted when attempting to locate the appropriate procedures to be used when shipping any substance or article.
[IMDG; International Maritime Dangerous Goods Code; International Maritime Organization p.6239 (1988)]**QC REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": Procurement ... of unduly large amt ... should be avoided. To avoid spilling, carcinogens should be transported in securely sealed glass bottles or ampoules, which should themselves be placed inside strong screw-cap or snap-top container that will not open when dropped & will resist attack from the carcinogen. Both bottle & the outside container should be appropriately labelled. ... National post offices, railway companies, road haulage companies & airlines

have regulations governing transport of hazardous materials. These authorities should be consulted before ... material is shipped. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 13]**QC REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": When no regulations exist, the following procedure must be adopted. The carcinogen should be enclosed in a securely sealed, watertight container (primary container), which should be enclosed in a second, unbreakable, leakproof container that will withstand chem attack from the carcinogen (secondary container). The space between primary & secondary container should be filled with absorbent material, which would withstand chem attack from the carcinogen & is sufficient to absorb the entire contents of the primary container in the event of breakage or leakage. Each secondary container should then be enclosed in a strong outer box. The space between the secondary container & the outer box should be filled with an appropriate quantity of shock-absorbent material. Sender should use fastest & most secure form of transport & notify recipient of its departure. If parcel is not received when expected, carrier should be informed so that immediate effort can be made to find it. Traffic schedules should be consulted to avoid ... arrival on weekend or holiday ... /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 13]**QC REVIEWED**

Storage Conditions:

Store separated from amines, alcohols, bases and acids.
[Handling Chemicals Safely 1980; 2nd Ed, Dutch Association of Safety Experts, the Dutch Chemical Industry Association and the Dutch Institute: 970]**PEER REVIEWED**

Storage temp: 75-100 deg F
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": Storage site should be as close as practicable to lab in which carcinogens are to be used, so that only small quantities required for ... expt need to be carried. Carcinogens should be kept in only one section of cupboard, an explosion-proof refrigerator or freezer (depending on chemicophysical properties ...) that bears appropriate label. An inventory ... should be kept, showing quantity of carcinogen & date it was acquired ... Facilities for dispensing ... should be contiguous to storage area. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC

Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 13]**PEER REVIEWED**

Cleanup Methods:

AQUEOUS SOLUTIONS CONTAINING 10-20% (WT) OF A NONIONIC SURFACTANT, ARKOPAL-N100, WAS A USEFUL DECONTAMINATING AGENT FOR TOLYLENE DIISOCYANATE (TDI). THE SOLUTION CAN BE SPRAYED DIRECTLY ON SPILLS AS A LIQUID OR MAY BE APPLIED IN THE FORM OF A FOAM WHICH CAN BE GENERATED IN SUITABLE FIRE EXTINGUISHING EQUIPMENT. SOLID DECONTAMINANT FORMULATIONS WERE ALSO DEVELOPED WHICH CAN BE USED FOR GROUND SPILLS OF TDI.
[IMPROVED DECONTAMINANT FOR TOLYLENE DIISOCYANATE (TDI); RES DISCL 193: 188 (1980)]**PEER REVIEWED**

Spillage: Neutralize with special mixt (50% water, 45% alc, 5% concn ammonia water), collect leaking liq in sealable containers (extra personal protection: self-contained breathing apparatus).
[Handling Chemicals Safely 1980; 2nd Ed, Dutch Association of Safety Experts, the Dutch Chemical Industry Association and the Dutch Institute: 970]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": A high-efficiency particulate arrestor (HEPA) or charcoal filters can be used to minimize amt of carcinogen in exhausted air ventilated safety cabinets, lab hoods, glove boxes or animal rooms ... Filter housing that is designed so that used filters can be transferred into plastic bag without contaminating maintenance staff is avail commercially. Filters should be placed in plastic bags immediately after removal ... The plastic bag should be sealed immediately ... The sealed bag should be labelled properly ... Waste liquids ... should be placed or collected in proper containers for disposal. The lid should be secured & the bottles properly labelled. Once filled, bottles should be placed in plastic bag, so that outer surface ... is not contaminated ... The plastic bag should also be sealed & labelled. ... Broken glassware ... should be decontaminated by solvent extraction, by chemical destruction, or in specially designed incinerators. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 15]**PEER REVIEWED**

Disposal Methods:

Generators of waste (equal to or greater than 100 kg/mo) containing this contaminant, EPA hazardous waste number U223, must conform with USEPA regulations in storage, transportation, treatment and disposal of waste.
[40 CFR 240-280, 300-306, 702-799 (7/1/91)]**PEER REVIEWED**

Toluene diisocyanate is a waste chemical stream constituent which may be subjected to ultimate disposal by controlled incineration. Controlled incineration: Oxides of nitrogen are removed from the effluent gas by scrubbers and/or thermal devices.
[USEPA; Engineering Handbook for Hazardous Waste Incineration p.2-10 (1981) EPA 68-03-3025]**PEER REVIEWED**

A potential candidate for rotary kiln incineration at a temperature range of 820 to 1,600 deg C and residence times of seconds for liquids and gases, and hours for solids. A potential candidate for liquid injection incineration at a temperature range of 650 to 1600 deg C and a residence time of 0.1 to 2 seconds. A potential candidate for fluidized bed incineration at a temperature range of 450 to 980 deg C and residence times of seconds for liquids and gases, and longer for solids.
[USEPA; Engineering Handbook for Hazardous Waste Incineration p.3-16 (1981) EPA 68-03-3025]**PEER REVIEWED**

This compound should be susceptible to removal from waste water by air stripping.
[USEPA/ORD; Innovative and Alternative Technology Assessment Manual pp.3-5, 3-11,12 (1980) EPA 430/9-78-009]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": There is no universal method of disposal that has been proved satisfactory for all carcinogenic compounds & specific methods of chem destruction ... published have not been tested on all kinds of carcinogen-containing waste. ... Summary of avail methods & recommendations ... /given/ must be treated as guide only. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 14]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": ... Incineration may be only feasible method for disposal of contaminated laboratory waste from biological expt. However, not all incinerators are suitable for this purpose. The most efficient type ... is probably the gas-fired type, in which a first-stage combustion with a less than stoichiometric air:fuel ratio is followed by a second stage with excess air. Some ... are designed to accept ... aqueous & organic-solvent solutions, otherwise it is necessary ... to absorb soln onto suitable combustible material, such as sawdust. Alternatively, chem destruction may be used, esp when small quantities ... are to be destroyed in laboratory. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 15]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": HEPA (high-efficiency particulate arrestor) filters ... can be disposed of by incineration. For spent charcoal filters, the adsorbed material can be stripped off at high temp & carcinogenic wastes generated by this treatment conducted to & burned in an incinerator. ... LIQUID WASTE: ... Disposal should be carried out by incineration at temp that ... ensure complete combustion. SOLID WASTE: Carcasses of lab animals, cage litter & misc solid wastes ... should be disposed of by incineration at temp high enough to ensure destruction of chem carcinogens or their metabolites. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 15]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": ... Small quantities of ... some carcinogens can be destroyed using chem reactions ... but no general rules can be given. ... As a general technique ... treatment with sodium dichromate in strong sulfuric acid can be used. The time necessary for destruction ... is seldom known ... but 1-2 days is generally considered sufficient when freshly prepd reagent is used. ... Carcinogens that are easily oxidizable can be destroyed with milder oxidative agents, such as sat soln of potassium permanganate in acetone, which appears to be a suitable agent for destruction of hydrazines or of compounds containing isolated carbon-carbon double bonds. Concn or 50% aqueous sodium hypochlorite can also be used as an oxidizing agent. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 16]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": Carcinogens that are alkylating, arylating or acylating agents per se can be destroyed by reaction with appropriate nucleophiles, such as water, hydroxyl ions, ammonia, thiols & thiosulfate. The reactivity of various alkylating agents varies greatly ... & is also influenced by sol of agent in the reaction medium. To facilitate the complete reaction, it is suggested that the agents be dissolved in ethanol or similar solvents. ... No method should be applied ... until it has been thoroughly tested for its effectiveness & safety on material to be inactivated. For example, in case of destruction of alkylating agents, it is possible to detect residual compounds by reaction with 4(4-nitrobenzyl)-pyridine. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 17]**PEER REVIEWED**

Occupational Exposure Standards:

NIOSH Recommendations:

Experimental studies have demonstrated that **toluene** and TDA (a hydrolysis product of **toluene** diisocyanate) are carcinogens. The test results meet both OSHA and NIOSH criteria for classifying a substance as a potential occupational carcinogen. NIOSH therefore recommends that all isomers of **toluene** diisocyanate and TDA be considered as potential carcinogens and that exposures be limited to the lowest feasible concn.
[ANON; USDHHS, Public Health Service, Centers for Disease Control, NIOSH, Division of Standards Development and Technology Transfer, 4676 Columbia Parkway, Cincinnati OH 45226, USA, 1989. 20p. Bibl.]**PEER REVIEWED**

NIOSH considers 2,4-**toluene** diisocyanate to be a potential occupational carcinogen. /2,4-**Toluene** diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

NIOSH usually recommends that occupational exposures to carcinogens be limited to the lowest feasible concentration. /2,4-**Toluene** diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

Immediately Dangerous to Life or Health:

NIOSH considers 2,4-**toluene** diisocyanate to be a potential occupational carcinogen. /2,4-**Toluene** diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

Manufacturing/Use Information:

Major Uses:

POLYURETHANE FOAMS, ELASTOMERS AND COATINGS; CROSS-LINKING AGENT FOR NYLON-6
[Sax, N.I. and R.J. Lewis, Sr. (eds.). Hawley's Condensed Chemical Dictionary. 11th ed. New York: Van Nostrand Reinhold Co., 1987. 1163]**PEER REVIEWED**

POLYURETHANE ELASTOMERS MADE FROM **TOLUENE** DIISOCYANATES ARE USED IN COATED FABRICS & CLAY-PIPE SEALS. **TOLUENE** DIISOCYANATES ARE ALSO USED IN ADHESIVES OF POLYURETHANE & OTHER TYPES. /**TOLUENE** DIISOCYANATES/
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V19 307 (1979)]**PEER REVIEWED**

POLYURETHANE COATINGS MADE FROM **TOLUENE** DIISOCYANATE MIXT ... IN GENERAL ... ARE USED IN FLOOR FINISHES, WOOD FINISHES & SEALERS, TRADE SALES PAINTS, CONCRETE SEALERS, & IN COATINGS FOR AIRCRAFT, TANK TRUCKS, TRUCK TRAILERS & TRUCK FLEETS. /MIXT OF 2,4- & 2,6-ISOMERS/
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V19 307 (1979)]**PEER REVIEWED**

... used as hardener in the production of polyurethane.
[Maki-Paakkanen J, Norppa H; Toxicol Lett 36 (1): 37-43 (1987)]**PEER REVIEWED**

Manufacturers:

BASF Corporation, Chemicals Division, 1255 Broad St., Cliftn, NJ 07015, (201) 316-2937 /**Toluene** 2,4- and 2,6-diiscyanate (80/20) mixture/

[United States International Trade Commission. Synthetic Organic Chemicals-United States Production and Sales, 1991. USITC Publication 2607, February 1993.Washington, DC: United States Trade Commission, 1993.,p. 3-8]**PEER REVIEWED**

ICI Americas, Inc., Polyurethane Group 286 Manuta Grove Road, W. Deptford, NJ 08066-1732. (609) 423-8300; Speciality Product Division Concord Pike & Murphy Rd, Willmington, DE 19897, (302) 886-3000 /**Toluene** 2,4- and 2,6-diisocyanate (80/20) mixture/
[United States International Trade Commission. Synthetic Organic Chemicals-United States Production and Sales, 1991. USITC Publication 2607, February 1993.Washington, DC: United States Trade Commission, 1993.,p. 3-8]**PEER REVIEWED**

Dow Chemical Co, 2020 Willard H. Dow Center, Midland, MI 48674, (517) 636-6125 /**Toluene** 2,4- and 2,6-diisocyanate (80/20) mixture/
[United States International Trade Commission. Synthetic Organic Chemicals-United States Production and Sales, 1991. USITC Publication 2607, February 1993.Washington, DC: United States Trade Commission, 1993.,p. 3-8]**PEER REVIEWED**

Olin Corporation, 120 Long Ridge Road, Stamford, CT 06904, (203) 356-2000 /**Toluene** 2,4- and 2,6-diisocyanate (80/20) mixture/
[United States International Trade Commission. Synthetic Organic Chemicals-United States Production and Sales, 1991. USITC Publication 2607, February 1993.Washington, DC: United States Trade Commission, 1993.,p. 3-8]**PEER REVIEWED**

Rubicon, Inc, PO Box 517, Geismar, LA 70734, (504) 673-6141 /**Toluene** 2,4- and 2,6-diisocyanate (80/20) mixture/
[United States International Trade Commission. Synthetic Organic Chemicals-United States Production and Sales, 1991. USITC Publication 2607, February 1993.Washington, DC: United States Trade Commission, 1993.,p. 3-8]**PEER REVIEWED**

Methods of Manufacturing:

NITRATION OF **TOLUENE**, FOLLOWED BY REDUCTION TO DIAMINE, REACTION WITH PHOSGENE, PURIFICATION, AND RECOVERY OF COPRODUCT HYDROGEN CHLORIDE.
[CHEM & ENG NEWS 63 (37): 16 (1985)]**PEER REVIEWED**

From **toluene** diamine by reaction with carbonyl chloride (phosgene)
[Zenz, C. Occupational Medicine-Principles and Practical Applications. 2nd ed. St. Louis, MO: Mosby-Yearbook, Inc, 1988. 1016]**PEER REVIEWED**

General Manufacturing Information:

MITSUBISHI CHEM CO IS DEVELOPING A PROCESS TO PRODUCE TDI BY CARBONYLATING DINITROTOLUENE IN THE PRESENCE OF AN ALCOHOL-PRODUCING

URETHANE THAT DECOMPOSES TO TDI AND THE ALCOHOL (THE ALCOHOL AND CARBON DIOXIDE CAN BE RECYCLED).
[CHEMICAL PRODUCTS SYNOPSIS: TOLUENE DIISOCYANATES, 1985]**PEER REVIEWED**

METHOD OF PURIFICATION: DISTILLATION TO REMOVE HYDROCHLORIC ACID.
[Sax, N.I. and R.J. Lewis, Sr. (eds.). Hawley's Condensed Chemical Dictionary. 11th ed. New York: Van Nostrand Reinhold Co., 1987. 1163]**PEER REVIEWED**

Formulations/Preparations:

GRADE: 100%-2,4 ISOMER; 80%:20%-2,4 & 2,6 ISOMER; 65%:35%-2,4 & 2,6 ISOMER
[Sax, N.I. and R.J. Lewis, Sr. (eds.). Hawley's Condensed Chemical Dictionary. 11th ed. New York: Van Nostrand Reinhold Co., 1987. 1163]**PEER REVIEWED**

Consumption Patterns:

90% FLEXIBLE FOAMS-MOLDED FLEXIBLE; 5% COATINGS; 3% ELASTOMERS; 2% OTHER (1984 EST) /FOR 80:20 MIX OF 2,4-2,6 ISOMER/
[CHEMICAL PRODUCTS SYNOPSIS: TOLUENE DIISOCYANATES, 1985]**PEER REVIEWED**

CHEMICAL PROFILE: **Toluene** Diisocyanate. Flexible urethane foams, 65%; (furniture, 28%; transportation, 16%; carpet underlay, 9%; bedding, 6%; other foam uses, 6%;) exports, 22%; rigid foams, 5%; polyurethane coatings, 4%; elastomers, 2%; miscellaneous non-foam uses, 2%.
[Kavaler AR; Chemical Marketing Reporter 232 (25): 50 (1987)]**PEER REVIEWED**

CHEMICAL PROFILE: **Toluene** diisocyanate. Demand: 1986: 650 million lb; 1987: 695 million lb; 1991 /projected/: 720 million lb (Includes exports, imports are negligible).
[Kavaler AR; Chemical Marketing Reporter 232 (25): 50 (1987)]**PEER REVIEWED**

80% 2,4:20% 2,6 MIXT REPRESENTS OVER 95% OF INDUSTRIAL USAGE ... .
[American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices. 5th ed. Cincinnati, OH:American Conference of Governmental Industrial Hygienists, 1986. 580]**PEER REVIEWED**

U. S. Production:

(1984) 3.32X10+11 g /80:20 MIX OF 2,4-2,6 ISOMERS/
[USITC. SYN ORG CHEM-U.S. PROD/SALES 1989 p.3-2]**PEER REVIEWED**

U. S. Imports:

(1983) 2.00X10+9 g /FOR 2,4 (AND 2,6) TDI/
[USITC. IMPORTS OF BENZENOID CHEMICALS & PRODUCTS 1983 p.29]**PEER

REVIEWED**

(1983) 8.94X10+8 g /FOR TDI (UNMIXED)/
[USITC. IMPORTS OF BENZENOID CHEMICALS & PRODUCTS 1983 p.29]**PEER REVIEWED**

(1983) 2.00X10+7 g /2,4 TDI DIMER/
[USITC. IMPORTS OF BENZENOID CHEMICALS & PRODUCTS 1983 p.29]**PEER REVIEWED**

U. S. Exports:

(1984) 6.27x10+10 g /**TOLUENE** DIISOCYANATES/
[BUREAU OF THE CENSUS. U.S. EXPORTS (1984) p.2-73]**PEER REVIEWED**

Laboratory Methods:

Analytic Laboratory Methods:

DETERMINATION OF **TOLUENE** DIISOCYANATE WORKING ATMOSPHERES BY HPLC USING UV OR FLUORESCENCE DETECTION. THE DETECTION LIMIT IS APPROX 1X10-4 MG/CU M.
[SANGOE C, ZIMERSON E; J LIQ CHROMATOGR 3 (7): 971 (1980)]**PEER REVIEWED**

DETERMINATION OF **TOLUENE** DIISOCYANATE (TDI) IN AIR BY LC. MAX SENSITIVITY IS OBSERVED AT AN EXCITATION WAVELENGTH OF 226 NM & USING A 300-NM CUT-OFF EMISSION FILTER. A DETECTION LIMIT OF 0.4 PPB FOR TDI CAN BE ACHIEVED WITH A 1 L AIR SAMPLE.
[KORMOS LH ET AL; ANAL CHEM 53 (7): 1122 (1981)]**PEER REVIEWED**

GASES IN THE ATMOSPHERE ARE MONITORED WITH CHEMICALLY-COATED QUARTZ PIEZOELECTRIC CRYSTALS; THE METHOD IS DEMONSTRATED IN THE USE OF POLYETHYLENE GLYCOL FOR **TOLUENE** DIISOCYANATE DETERMINATION. A MICROPROCESSOR IS USED TO CONTROL THE GAS SAMPLE FLOW THROUGH THE DETECTOR HEAD AS WELL AS THE DATA ACQUISITION. THE THEORETICAL DETECTION LIMIT IS APPROX 0.006 PPM.
[ALDER JF, ISAAC CA; ANAL CHIM ACTA 129 (1): 175 (1981)]**PEER REVIEWED**

TOLUENE DIISOCYANATE ... DETERMINED IN ... ATMOSPHERE BY TLC.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V19 309 (1979)]**PEER REVIEWED**

Matrix: Air. Sample preparation: Draw air through impinger containing aq acid; diazotize (NaNO2/NaBr); decompose excess nitrous acid; react with N-(1-naphthyl)-ethylenediamine. Procedure: colorimetric. Limit of detection: 50 ug/cu m. /From table/

[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 300 (1986)]**PEER REVIEWED**

Matrix: Air. Sample preparation: Draw air through tube containing glass wool coated with N-para-nitrobenzyl-N-propylamine; extract (dichloromethane). Procedure: HPLC/UV. Limit of detection: 4 ug/cu m. /From table/
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 300 (1986)]**PEER REVIEWED**

Matrix: Air. Sample preparation: Draw air through impinger containing ethanol. Procedure: HPLC/UV. Limit of detection: 1-5 ug/cu m, /From table/
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 300 (1986)]**PEER REVIEWED**

Matrix: Air. Sample preparation: Draw air through impinger containing aq acid; neutralize; extract (chloroform or **toluene**); react with trifluoroacetic anhydride or heptafluorobutyric anhydride. Procedure: GC/ECD. Limit of detection: 1-5 ug/cu m. /From table/
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 300 (1986)]**PEER REVIEWED**

Matrix: Polymer. Sample preparation: Extract (ortho-dichlorobenzene). Procedure: GC/FID. Limit of detection: 5 ug/g. /From table/
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 300 (1986)]**PEER REVIEWED**

An electrochemical detection for TDI in air, using 1-(2-methoxyphenyl)piperazine as the electrogenic reagent, was significantly more sensitive than high-performance liq chromatography-uv detection methods.
[Warwick CJ et al; Analyst 106 (June): 676-85 (1981)]**PEER REVIEWED**

A reversed-phase HPLC using a 1-(2-pyridyl)piperazine reagent was described for the determination of TDI in air.
[Goldberg PA et al; J Chromatogr 212 (1): 93-104 (1981)]**PEER REVIEWED**

NIOSH Method: 5521. Analyte: 2,6-**Toluene** diisocyanate. Matrix: Air. Procedure: High performance liquid chromatography, electrochemical and ultra violet detection. For 2,6-**toluene** diisocyanate this method has an estimated detection limit of ca. 0.1 ug diisocyanate/sample. The precision/RSD is not

determined and the recovery is not given. Applicability: The working reange is from ug/cu m to more than 1 mg/cu m for a 100 liter air samples. Interferences: Any cmpd which elutes with ureas and absorbs ultraviolet light or is electroactive will interfere with the analysis. /2,6-**Toluene** diisocyanate/
[U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. 5521-1]**PEER REVIEWED**

NIOSH Method: 5505. Analyte: 1-(2-methoxyphenyl)piperazine; NCO group. Matrix: Air. Procedure: High performance liquid chromatography, ultra violet detection. For 1-(2-methoxyphenyl)piperazine; NCO group, this method's estimated detection limit is not determined. The precision/RSD is 0.048 and the recovery is 96%. Applicability: This method determines the total concn of isocyanates, regardless of the identities of the specific cmpd present. Interferences: Phosgene, acid halides, and possibly some esters will react with 1-(2-methoxyphenyl)piperazine and thus cause a positive bias. /Isocyanate group/
[U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. 5505-1]**PEER REVIEWED**

Isocyanate determination air paper tape Hydrazine determination air paper tape;Air analysis Hydrazine deriv. and **toluene** diisocyanate determination. in, miniature paper tape apparatus for
[Hughes WT Jr; Anal Instrum (Research Triangle Park, N. C.) 22: 87-98 (1986)]**PEER REVIEWED**

A passive monitor for **toluene** diisocyanate which utilizes microporous Teflon diffusion membranes and a 0.5% sulfuric acid absorbing medium was evaluated. The collection rate of **toluene** diisocyanate is proportional to exposure dose from 10 to at least 300 ppb.hr, and response is equivalent for 2,4- and 2,6-**toluene** diisocyanate. Collection rate is independent of humidity and normal atmospheric pressure variations, while temperature causes a decrease of 1.0% per deg C. Negative interference caused by ambient nitrogen dioxide is eliminated by addition of sulfamic acid to the collecting medium. N-Ethylmorpholine is a positive interferent. Field testing of the sampler against a reference impinger technique indicated a positive bias when **toluene** diisocyanate is aerosolized.
[Rando RJ et al; Am Ind Hyg Assoc J 50 (1): 8-14 (1989)]**PEER REVIEWED**

A solvent free sampling method for airborne **toluene** diisocyanate was described. Air samples were collected on quartz fiber filters impregnated with 1-(2-methoxyphenyl)piperazine. **Toluene** diisocyanate in the samples reacted with 1-(2-methoxyphenyl)piperazine to form urea derivatives which after dissolution in methanol were analyzed by reversed or normal phase HPLC. When reversed phase HPLC was used, a C18 bonded phase column was utilized. A cyano amino bonded phase column was used with normal phase HPLC. An ultraviolet detector set at a wavelength 250 nanometers was also used. Detection limits for a 15 liter air sample based on a 5 mm peak height were 0.02 to 0.04 mg/cu m, corresponding to 0.5 to 1 nanograms of **toluene** diisocyanate injected. The method was used to sample laboratory generated **toluene** diisocyanate containing atmospheres over the relative humidity range 11 to 75% and temperature range 20 to 50 deg C. In the study of the effects of humidity, samples were also

collected with gas bubblers and silica gel tubes for comparison purposes. **toluene** diisocyanate concn in the collected samples increased linearly with incr temperature. When the samples were collected on the 1-(2-methoxyphenyl)piperazine coated fibers the collected **toluene** diisocyanate concn were not affected by changes in relative humidity. Collection efficiency of the bubblers and silica gel tubes decr for humidities in excess of 45%. It was concluded that the 1-(2-methoxyphenyl)piperazine impregnated quartz fiber filter method for **toluene** diisocyanate sampling is convenient and efficient, and that collection efficiency does not appear to be affected by humidity.
[Robert A, Simon P; Chromatographia 23 (7):507-11 (1987)]**PEER REVIEWED**

Sampling Procedures:

THE RESPONSE OF A DUNLOP/ICI CONTINUOUS TDI MONITOR WAS EVALUATED USING THE NIOSH MODIFIED MARCALI SPECTROPHOTOMETRIC METHOD AS THE REFERENCE PROCEDURE.
[MILLER JA, MUELLER FX; AM IND HYG ASSOC J 36 (6): 477-83 (1975)]**PEER REVIEWED**

AN ANALYTICAL METHOD FOR THE CALIBRATION OF A CONTINUOUS 701 MONITOR USING A DIFFUSION CELL TO GENERATE CONSTANT CONCN OF TDI IS DESCRIBED. APPLICATION TO OCCUPATIONAL EXPOSURE MONITORING IS DISCUSSED.
[NEILSON A, BOOTH KS; AM IND HYG ASSOC J 36 (3): 1969-71 (1975)]**PEER REVIEWED**

Matrix: Air. Procedure: Draw air through impinger containing aq acid or through tube containing glass wool coated with N-para-nitrobenzenyl-N-propylamine or through impinger containing ethanol. /From table/
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 300 (1986)]**PEER REVIEWED**

Matrix: Polymer. Procedure: Extract (ortho-dichlorobenzene) /From table/
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 300 (1986)]**PEER REVIEWED**

EPA Method 8020. For the analysis of solid waste, a representative sample (solid or liquid) is collected in a standard 40 ml glass screw cap VOA vial equipped with a Teflon faced silicone septum. Sample agitation, as well as contamination of the sample with air, must be avoided. Two vials are filled per sample location, then placed in separate plastic bags for shipment and storage. /**Toluene**/
[USEPA; Test Methods for Evaluating Solid Waste SW-846 (1986)]**PEER REVIEWED**

NIOSH Method: 5521. Analyte: 2,6-**Toluene** diisocyanate. Matrix: Air. Sampler: Impinger (solution of 1-(2-methoxyphenyl)-piperazine in **toluene**). Flow Rate: 1 l/min. Sample Size: 100 liters. Shipment: Ship in screw-cap vial refrigerated @ 4 deg C or lower. Sample Stability: May be unstable; perform steps 8

and 9 as soon as possible. /2,6-**Toluene** diisocyanate/
[U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. 5521-1]**PEER REVIEWED**

NIOSH Method: 5505. Analyte: 1-(2-methoxyphenyl)piperazine; HCO group. Matrix: Air. Sampler: Impinger (solution of 1-(2-methoxyphenyl)-piperazine in **toluene**). Flow Rate: 1 l/min. Sample Size: 600 liters. Shipment: In vials; flammable liquid. Sample Stability: Equal to or greater than 2 weeks. /Isocyanate group/
[U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. 5505-1]**PEER REVIEWED**

A solvent free sampling method for airborne **toluene** diisocyanate was described. Air samples were collected on quartz fiber filters impregnated with 1-(2-methoxyphenyl)piperazine. When the samples were collected on the 1-(2-methoxyphenyl)piperazine coated fibers, the collected **toluene** diisocyanate concn were not affected by changes in relative humidity.
[Robert A, Simon P; Chromatographia 23 (7):507-11 (1987)]**PEER REVIEWED**

Special References:

Special Reports:

Santodonato J et al; Report ISB SRC-TR-85-189 Order No PB86-180213/gar (1985)

Davies RJ; Clinics in Immunology and Allergy 4 (1): 103-23 (1984) Respiratory Hypersensitivity To Diisocyanates

Kay S; Food and Chemical Toxicology 23 (3): 411-13. (1985) **Toluene** diisocyanate and Lung Function.

Toluene diisocyanate; Safety Practitioner 3 (5): 32-3 (1985).

DHHS/NTP; Toxicology & Carcinogenesis Studies of Commercial Grade 2,4 (80%)- and 2,6 (20%)-**Toluene** Diisocyanate in F344/N Rats and B6C3F1 Mice(Gavage Studies) Technical Report Series No. 251 (1986) NIH Publication No. 86-2507

U.S. Department of Health & Human Services/National Toxicology Program; 8th Report on Carcinogens. National Institute of Environmental Health Sciences, Research Triangle Park, NC. (1998)

... The toxicity of inhaled vapors of diisocyanates is summarized.
[Davies RJ; Clinics in Immunology and Allergy 4 (1): 103-23 (1984)]

Synonyms and Identifiers:

Related HSDB Records:

874 [2,4-**TOLUENE** DIISOCYANATE] (Mixture Component)

5272 [2,6-**TOLUENE** DIISOCYANATE] (Mixture Component)

Synonyms:

BENZENE, 1,3-DIISOCYANATOMETHYL-
PEER REVIEWED

DIISOCYANATOTOLUENE
PEER REVIEWED

HYLENE T
PEER REVIEWED

ISOCYANIC ACID, METHYL-M-PHENYLENE ESTER
PEER REVIEWED

METHYLPHENYLENE ISOCYANATE
PEER REVIEWED

METHYL-M-PHENYLENE ISOCYANATE
PEER REVIEWED

MONDUR TD
PEER REVIEWED

MONDUR TD-80
PEER REVIEWED

TDI
PEER REVIEWED

TOLYLENE DIISOCYANATE
PEER REVIEWED

TOLYLENE ISOCYANATE
PEER REVIEWED

Formulations/Preparations:

GRADE: 100%-2,4 ISOMER; 80%:20%-2,4 & 2,6 ISOMER; 65%:35%-2,4 & 2,6 ISOMER
[Sax, N.I. and R.J. Lewis, Sr. (eds.). Hawley's Condensed Chemical Dictionary. 11th ed. New York: Van Nostrand Reinhold Co., 1987. 1163]**PEER REVIEWED**

Shipping Name/ Number DOT/UN/NA/IMO:

UN 2078; **Toluene** diisocyanate

IMO 6.1; **Toluene** diisocyanate

Standard Transportation Number:

49 215 75; **Toluene** diisocyanate

EPA Hazardous Waste Number:

U223; A toxic waste when a discarded commercial chemical product or manufacturing chemical intermediate or an off-specification commercial chemical product or a manufacturing chemical intermediate.

RTECS Number:

NIOSH/NQ9490000

Administrative Information:

Hazardous Substances Databank Number: 6003

Last Revision Date: 20000929

Last Review Date: Reviewed by SRP on 9/24/1992

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Field update on 01/11/1993, 1 field added/edited/deleted.
Field Update on 11/20/1992, 1 field added/edited/deleted.
Complete Update on 04/01/1992, 1 field added/edited/deleted.
Complete Update on 09/26/1991, 1 field added/edited/deleted.
Complete Update on 07/18/1991, 1 field added/edited/deleted.
Complete Update on 10/23/1990, 3 fields added/edited/deleted.

Field Update on 08/23/1990, 1 field added/edited/deleted.
Field Update on 05/04/1990, 1 field added/edited/deleted.
Complete Update on 04/13/1989, 2 fields added/edited/deleted.
Field Update on 03/01/1989, 1 field added/edited/deleted.
Complete Update on 12/28/1988, 83 fields added/edited/deleted.
Complete Update on 10/03/1986

Record Length: 225484

TOLUENE DIISOCYANATE

CASRN: 26471-62-5

For other data, click on the Table of Contents

Human Health Effects:

Evidence for Carcinogenicity:

No data are available in humans. Sufficient evidence of carcinogenicity in animals. OVERALL EVALUATION: Group 2B: The agent is possibly carcinogenic to humans.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. S7 72 (1987)]**PEER REVIEWED**

Human Toxicity Excerpts:

TOLUENE DIISOCYANATE (TDI) SENSITIVITY ACCOMPANIED BY NONSPECIFIC BRONCHIAL HYPERRESPONSIVENESS OCCURS IN 5% OF OCCUPATIONALLY EXPOSED WORKERS. THE CASE OF A 32 YR OLD WORKER FOLLOWED LONGITUDINALLY AFTER REMOVAL FROM ISOCYANATE EXPOSURE IS REPORTED. TDI REACTIVITY WAS LOST 11 MONTHS AFTER REMOVAL FROM EXPOSURE & NONSPECIFIC BRONCHIAL HYPERRESPONSIVENESS RESOLVED AFTER 17 MONTHS. IMMUNOPHARMACOLOGIC RESULTS SHOW THAT THE WORKER'S INITIAL DECREASED ABILITY OF LYMPHOCYTES TO PRODUCE CYCLIC-AMP RETURNED TO NEAR NORMAL AFTER 2 YR. IMMUNOGLOBULIN-E ANTIBODIES TO A HUMAN SERUM ALBUMIN TOLYL MONOISOCYANATE CONJUGATE WERE STILL PRESENT THIS TIME.
[BUTCHER BT ET AL; J ALLERGY CLIN IMMUNOL 70 (4): 231 (1982)]**PEER REVIEWED**

ACCIDENTAL SPLASH ... IN EYES OF WORKMEN HAS CAUSED KERATITIS & CONJUNCTIVITIS. ONE CASE ... DESCRIBES "UNUSUAL AMT OF PHOTOPHOBIA & BLEPHAROSPASM" ... SECOND CASE ... INVOLVED SEVERE IRIDOCYCLITIS & SECONDARY GLAUCOMA.
[Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986. 929]**PEER REVIEWED**

WORKERS EXPOSED ... DEVELOPED IRRITATION OF EYES, IRRITATION OR DRYNESS OF THROAT &/OR TIGHTNESS OF CHEST. EXPOSURE TO LEVELS AS LOW AS 0.014 MG/CU M (0.002 PPM) CAN RESULT IN CHRONIC LOSS OF PULMONARY FUNCTION. MORE ACUTE, ASTHMATIC TYPE OF BRONCHITIS IS ... TYPICAL, FRANK ASTHMA MAY OCCUR.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V19 311 (1979)]**PEER REVIEWED**

RESP SYMPTOMS ... IMPROVE ... AFTER REMOVAL FROM /OCCUPATIONAL/ EXPOSURE, BUT ... RE-EXPOSURE TO EVEN MINIMAL CONCN ... PRODUCED RECURRENCE OF ...

SYMPTOMS. HYPERSENSITIVITY ... ARISES AFTER ... INHALATION, & IT HAS BEEN RELATED TO IMMUNOLOGICAL CHANGES ... & TO ALTERED BETA-ADRENERGIC FUNCTION.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V19 311 (1979)]**PEER REVIEWED**

... DOSE-RESPONSE RELATIONSHIP OF ACUTE PULMONARY FUNCTION CHANGES AMONG 112 WORKERS EXPOSED ... TO 0.0035-0.06 MG/CU M (0.0005-0.009 PPM). 2-YR FOLLOW-UP EXAM OF 57 OF WORKERS DISCLOSED DECR IN PULMONARY FUNCTION ... RELATED TO EXPOSURE LEVELS, CONTROLLING FOR AGE, MO EMPLOYED, SMOKING ... & PHYSIQUE.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V19 311 (1979)]**PEER REVIEWED**

A series of workers with exposure to and respiratory symptoms from **toluene** diisocyanate was compared with a group of exposed, asymptomatic workers and with normal controls using immunologic and clinical evaluations. Improved understanding of **toluene** diisocyanate-induced respiratory disease may best be achieved by categorizing the symptomatic workers into at least 3 and possibly 4 groups: immunologic asthma; pre-existing chronic respiratory disease exacerbated or unaffected by **toluene** diisocyanate; asthma coincidental with exposure, and possibly respiratory disease secondary to toxic or inflammatory mechanisms.
[Patterson R et al; Int Arch Allergy Appl Immunol 84 (1): 93-100 (1987)]**PEER REVIEWED**

Subjects exposed to 0.0010 to 0.0015 ppm of **toluene** diisocyanate demonstrated a normal age and smoking-related rate of decline in forced expiratory volume in 1 second and no evidence that it was related to isocyanate exposures.
[Musk AW et al; J Occup Med 27 (12): 917-20 (1985)]**PEER REVIEWED**

Twelve subjects were studied with inhalation challenge testing to **toluene** diisocyanate because of suspected asthma based on a consistent clinical and occupational history. In seven cases, asthma was documented by a positive inhalation challenge to low levels of **toluene** diisocyanate. Six of the seven reactors had persistent respiratory symptoms and required daily treatment even though they had been removed from isocyanate exposure for intervals as long as 12 years (mean 4.5 years). These six reactors had either dual (four cases) or late bronchospasm (two cases) to less than 20 ppb and all had a positive methacholine or cold air challenge prior to study. The one reactor with a negative methacholine challenge had a positive (immediate) bronchospastic response to a challenge performed one week after removal from isocyanate exposure. Five workers had a negative challenge, two of whom had persistent respiratory symptoms and positive methacholine challenges at the time of inhalation testing. ... Respiratory symptoms may persist following long-term removal from occupational exposure to and are associated with nonspecific bronchial hyperreactivity. The sensitivity may also persist for a long time even in the absence of any additional occupational exposure. Long-term prospective studies of symptomatic isocyanate workers are needed to fully define the extent of this problem.

[Moller DR et al; Chest 90 (4): 499 (1986)]**PEER REVIEWED**

Two workers who developed asthmatic symptoms were studied with inhalation provocation tests using ... **toluene** diisocyanate. Subjects did not show asthmatic reations to TDI challenge.
[Mapp CE et al; Ann Allergy 54 (5): 424-9 (1985)]**PEER REVIEWED**

Amine induced asthma was studied in polyurethane foam workers. A total of 12 subjects, occupationally exposed to polyurethane foams, who complained of wheezing and breathlessness at work were tested. Subjects were given 20 to 2000 ug methacholine. Forced expiratory volume in 1 sec was measured. Subjects were challenged with 0.01 ppm **toluene** diisocyanate for 15 min in an atmosphere chamber. Forced expiratory volume in 1 sec was measured. Positive tests were considered as a 15% fall in forced expiratory volume in 1 sec. High sensitivity to methacholine was seen in ten subjects with a 15% fall in forced expiratory volume in 1 sec at <1000 ug; normal subjects responded at 2000 ug. All subjects reacted to **toluene** diisocyanate.
[Cardura F, Moscata G; Brit J Indus Med 41: 552-3 (1984)]**PEER REVIEWED**

... The toxicity of inhaled vapors of diisocyanates is summarized. Humans are exposed to high concentrations of diisocyanates in polyurethane industries. Toxic symptoms are acute inflammation with lachrymation, rhinitis, soreness and burning in the throat and upper part of the chest, and coughing. Fire fighters are particularly prone to these clinical symptoms. The toxic limit value for **toluene** diisocyanate is 0.005 ppm. Exposure to diisocyanates can cause asthma.
[Davies RJ; Clinics in Immunology and Allergy 4 (1): 103-23 (1984)]**PEER REVIEWED**

The respiratory status of factory workers exposed continously to isocyanates over 10 years was studied. A total of 80 workers in two facilities that manufactured fixtures used in the interiors of cars were examined and underwent spirometry before and after work. Of these, 12 were comparisons not exposed to **toluene** diisocyanate. Subjects included those previously examined in 1971. Ventilatory capacity tests were performed inlcuding forced expiratory volume in 1 sec and forced vital capacity testing. Annual decrements were calculated. The mean average concentration of **toluene** diisocyanate was not more than 0.0033 ppm respectively. Subjects who had been studied previously had a mean forced vital capacity of 104.6% and a mean forced expiratory volume in 1 sec of 107% of predicted values. Three subjects with significant obstruction in the lung function tests were smokers. The comparisons in facility 1 had a significantly lower percentage of the predicted forced fital capacity and forced expiratory volume than the exposed population. Most of the data from 1971 for annual decrement calculations were not reliable. A 10% decrement in forced vital capacity and forced expiratory volume in 1 second was indicative of significant postshift decline and would indicate the presence of isocyanate asthma or hypersensitivity; no subject at either facility met the criteria.
[Gee JB; Morgan WKC; J Occup Med 27 (1): 15-8 (1985)]**PEER REVIEWED**

The mechanism by which late asthmatic reactions are induced by **toluene** diisocyanate, a low molecular weight chemical that causes occupational asthma in exposed subjects, is unknown. An investigation was conducted to determine whether early and late asthmatic reactions induced by **toluene** diisocyanate are associated with changes in airway responsiveness to methacholine and airway inflammation as determined by bronchoalveolar lavage. Forced expiratory volume in 1 second was measured before and at regular intervals after exposure to **toluene** diisocyanate and dose-response curves to methacholine and

bronchoalveolar lavage at 8 hr after **toluene** diisocyanate /were performed/ in a group of 6 subjects with late asthmatic reactions and in 6 subjects with only early asthmatic reactions. The same procedure was followed 2 hr after **toluene** diisocyanate in a group of 6 subjects with previously documented late asthmatic reactions and in a group of 6 subjects without any previously documented asthmatic reaction after **toluene** diisocyanate. In subjects with late asthmatic reactions, neutrophils were increased at both 2 hr and 8 hr and eosinophils and airway responsiveness were increased only at 8 hr. By contrast, neutrophils, eosinophils and airway responsiveness were not increased at 8 hr after **toluene** diisocyanate in subjectswith an early asthmatic reaction or at 2 hr after **toluene** diisocyanate in normal control subjects. These results suggest that late asthmatic reactions to **toluene** diisocyanate, and the associated increase in airway responsiveness may be caused by airway inflammation.
[Fabbri LM et al; Am Rev Respir Dis 136 (1): 36-42 (1987)]**PEER REVIEWED**

Technical grade **toluene** diisocyanate induced chromosome aberrations after a 24 hr treatment in the absence of metabolic activation in human whole blood lymphocyte cultures.
[Maki-Paakkanen J, Norppa H; Toxicol Lett 36 (1): 37-43 (1987)]**PEER REVIEWED**

To determine whether late asthmatic reactions and the associated increase in airway induced by **toluene** diisocyanate are linked to airway inflammation, inhibition by prednisone was investigated. Ten "sensitized" subjects were studied in 2 sets of experiments. In the first set, each subject was given no treatment and was studied before and for 8 hr after exposure to **toluene** diisocyanate. In the second set, 2 to 4 wk later, each subject was studied before treatment and then during treatment with prednisone (50 mg once a day for 3 days, orally), both before and after exposure to **toluene** diisocyanate. To assess late asthmatic reactions to **toluene** diisocyanate FEV1 /was measured/ immediately before and after exposure, then hourly for 8 hr. To assess changes in airway responsiveness, a /measurement was made of/ the provocation dose (mg) of methacholine causing a 20% decrease in FEV1 (PD20FEV1) before and 8 hr after exposure to **toluene** diisocyanate. When the subjects received no prednisione treatment, **toluene** diisocyanate caused late asthmatic reactions and increased airway responsiveness. By contrast, when the subjects received prednisone, **toluene** diisocyanate caused no late asthmatic reaction or increased airway responsiveness. Prednisone did not change baseline airway caliber or airway responsiveness. These results suggest that late asthmatic reactions and the associated increase in airway responsiveness induced by **toluene** diisocyanate in "sensitized" subjects may depend on the development of a steroid-responsive acute inflammatory reaction within the airways.
[Fabbri LM; Am Rev Respir Dis 132 (5): 1010-4 (1985)]**PEER REVIEWED**

Case reports of keratophathy in polyurethane production workers were examined. The experimental production of similar conditions was studied in cats and a monkey. A male polyurethane worker complained of blurred vision which improved over weekends away from work. The only significant finding on examination of the eyes was subepithelial corneal vesicles of 30 to 50 micrometers in diameter. A second patient, a female worker from the same facility, also complained of attacks of blurred vision. Slit lamp examination showed deep or subepithelial vacuolization only in the palpebral aperture. ... Corneas were normal between 3 day and 2 weeks. Exposure to **toluene** diisocyanate did not result in the clinical appearance of the eye resembling that of the workers.
[Potts AM et al; Am J Indust Med 9 (2): 203-13 (1986)]**PEER REVIEWED**

Symptoms and lung function of workers exposed to isocyanates in polyurethane foam factories were studied. A group of 67 workers was examined for **toluene**-diisocyanate ... exposure. Measurements were made by samples obtained from subject carried pumps. Interviews were also conducted for information of symptoms involving the nose, eyes, upper airways, and lung. Another group of 56 nonexposed workers was determined by spirometry and nitrogen wash out prior to the work shift. The exposed workers were examined again immediately after work. The variables studied were forced expired vital capacity and forced expired volume in 1 second. ... The highest exposure group was foaming machine workers, with a day mean exposure of 0.023 mg/cu m. Nonsmokers showed an increased frequency of symptoms involving the nose, throat, and dyspnea. Smokers had no significant increase. Smokers of the exposed group reported coughing. Only smokers reported symptoms classified as chronic bronchitis, with frequency independent of exposure. Decreased forced expired vital capacity and forced expired volume were observed in the exposed group. This group also showed increased expired vital capacity. Lung function impairment was restricted to smokers. Spirometric and nitrogen washout variables did not change significantly during the work shift. Decreasing spirometric values with increased exposure was seen in smokers. Conclusions indicate that mean exposure of 0.01 mg/cu m/day to isocyanates may give an increased frequency of symptoms in nonsmokers.
[Alexanderson R et al; Internat Archives of Occup Environ Health 55 (2): 149-57 (1985)]**PEER REVIEWED**

A survey of the incidence of occupational asthma in a steel coating factory was conducted. The survey was prompted by two male employees developing symptoms suggestive of occupational asthma. The cohort consisted of 221 males employed in the coating shop. A respiratory questionnaire was administered. Spirometric tests were conducted. Peak expiratory flow rate studies were performed on 50 subjects. Twenty one subjects reported symptoms of occupational asthma. Sixty three had other work related symptoms and 58 had respiratory symptoms unrelated to work. The mean length of employment of the subjects with asthmatic symptoms was 7.7 years. All symptomatic subjects had significantly reduced 1 second forced expiratory volumes, compared to asymptomatic workers. 21% of the peak expiratory flow rates were indicative of work related asthma. Two symptomatic subjects were administered inhalation challenge tests with **toluene** diisocyanate after it was discovered that one of the coatings that had been used for 8 years released **toluene** diisocyanate during the coating process. Both subjects showed decreases in forced expiratory volumes of at least 15% below the baseline values. Environmental sampling for **toluene** diisocyanate indicated concentrations ranging from below 0.001 to 0.026 ppm. The coating containing **toluene** diisocyanate was removed from the process. A follow-up survey conducted 1 year later showed that 17 of the symptomatic subjects had become asymptomatic or improved.
[Venables KM et al; Brit J Indus Med 42 (8): 517-24 (1985)]**PEER REVIEWED**

The presence of different thresholds on bronchial reactivity to **toluene** diisocyanate was tested in 20 spray painters employed in the furniture industry and affected by TDI induced asthma. Bronchial provocation tests failed to demonstrate nonspecific hyperreactivity to methacholine. Exposure of the workers to **toluene** diisocyanate in concentrations ranging from 0.02 to 0.25 ppm demonstrated the occurrence of low, moderate and high thresholds of airways response to **toluene** diisocyanate in nine, seven and four patients, respectively. There was no association between the **toluene** diisocyanate response threshold and the positive response pattern to the lower range of **toluene** diisocyanate levels, but six of the nine patients with low threshold of response to **toluene** diisocyanate and six of the 11

patients with moderate or high thresholds had nonspecific bronchial hyperreactivity. The response to **toluene** diisocyanate also was not associated with the duration of the asthmatic condition, smoking, cessation of work or nonspecific response to methacholine. The pattern of response was not dose dependent in ten of 13 patients who had two positive bronchial provocation tests with different levels of **toluene** diisocyanate, although dual responses were recorded in three patients who had late reactions at low concentrations of **toluene** diisocyanate. The value of forced expiratory volume in one second, recorded during immediate reactions, showed a dose response relationship, in that it declined by 28.4% at lower **toluene** diisocyanate levels as compared to 38.3% following inhalation of higher doses of the compound; no such association was established for the late reaction to **toluene** diisocyanate. The results conclude that patients who are sensitive to **toluene** diisocyanate may have different thresholds of response to the agent.
[Paggiaro PL et al; Respiration 50 (3): 167-73 (1986)]**PEER REVIEWED**

Respiratory variables were measured in workers exposed to **toluene** diisocyanate in Canada. Exposure and effect relationships were studied. Results from 95 isocyanate workers were compared with unexposed workers. Exposed workers were grouped according to production areas based on isocyanate concentrations measured. Individual monitors were worn to identify exposure for some workers. Symptoms and history of respiratory illness were compared through questionnaires. Pulmonary function tests included forced vital capacity, forced expiratory volume in 1 second, and forced expiratory flow at 50% and 75% of vital capacity. Pulmonary function was measured at the beginning and end of work shifts on Monday, Wednesday, and Friday of a work week. Regression analysis of exposure concentration and other variables was attempted. When comparisons were adjusted for smoking habits, exposed workers had a significantly lower family history of respiratory complaints. Isocyanate workers had slightly lower base line lung function than comparisons, but had significantly higher declines in pulmonary function over the work week. A 5% or greater decline over a day occurred in 44 percent of exposed but only 22% of comparison workers. Foam line and finishing area workers had greatest declines in forced vital capacity and forced expiratory volume in 1 second. It was concluded that although regression analysis does not show an exposure/effect relationship, an all or none effect may be operating with acute and chronic compartments. However, sample size may have been insufficient.
[Holness DL et al; J Occup Med 26 (6): 449-55 (1984)]**PEER REVIEWED**

Toluene diisocyanate may produce a true hemorrhagic syndrome affecting the bone marrow and producing primarily thrombocyte series suppression.
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 303]**PEER REVIEWED**

All workers develop eye, nose, and throat irritation at 0.5 ppm. Sensitized individuals may manifest symptoms at levels as low as 0.02 ppm.
[Ellenhorn, M.J. and D.G. Barceloux. Medical Toxicology - Diagnosis and Treatment of Human Poisoning. New York, NY: Elsevier Science Publishing Co., Inc. 1988. 880]**PEER REVIEWED**

A worker developed **toluene** diisocyanate induced asthma in 1974. On reassessment, 11 yr after leaving the chemical plant where **toluene** diisocyanate was produced, he had no respiratory symptoms and normal bronchial reactivity in response to methacholine, and showed no reaction when challenged with a

subirritant concn of **toluene** diisocyanate. He developed asthma within five months of returning to the workplace. Repeat challenge testing showed bronchial hyperreactivity to methacholine and to the specific sensitising agent, **toluene** diisocyanate. This clinical pattern could be due to underlying **toluene** diisocyanate sensitivity with resolution and reappearance of hyperresponsiveness to methacholine and **toluene** diisocyanate reactivity associated with workplace **toluene** diisocyanate exposure. Alternatively, this worker may have developed sensitisation to **toluene** diisocyanate anew.
[Banks DE, Rando RJ; Thorax 43 (8): 1988 660-2]**PEER REVIEWED**

An investigation of the persistence of isocyanate induced asthma in workers with negligible occupational exposure was carried out. Six asthmatic workers, proven to be **toluene** diisocyanate sensitive by inhalation challenge testing in a longitudinal study of respiratory health risks associated with polyurethane foam production, were examined. The subjects were followed for 5 yr during which they completed a respiratory symptom questionnaire annually. Pulmonary function and responsiveness to methacholine challenge were measured annually. **toluene** diisocyanate concn in their breathing zones were measured. After the original survey the six subjects were transferred to areas thought to have negligible **toluene** diisocyanate exposures. None of the subjects had respiratory or asthmatic complaints before they started work in polyurethane production. The respiratory symptoms of the subjects did not improve during the followup period. All six had bronchial hyperresponsiveness to methacholine that did not resolve over time. Three subjects demonstrated deficits in 1 second forced expiratory volume of greater than 15% on one of the testing days during the followup period. The need for less or additional asthma therapy of the subjects could not be predicted. The mean time weighted average **toluene** diisocyanate exposure experienced by the subjects was 0.64 ppb; less than 5% of the OSHA standard of 20 ppb. It was concluded that although the outcome of isocyanate induced asthma cannot be predicted, the asthmatic symptoms of these workers have persisted despite the negligible **toluene** diisocyanate exposures.
[Banks DE et al; Chest 97 (1): 121-5 (1990)]**PEER REVIEWED**

The prevention of airway inflammation caused by **toluene** diisocyanate by prednisone was studied. Healthy **toluene** diisocyanate sensitive individuals were exposed to 0.018 ppm **toluene** diisocyanate in a test chamber. Bronchoalveolar lavage fluid was collected with a flexible fiberoptic bronchoscope. The lavage fluid was spun in a cytocentrifuge and stained with May/Grunwald/Giemsa for differential cell count. The total cell count was performed on resuspended cell pellets. A late asthmatic response was characterized by the occurrence of less than 20% of free expiratory volume in 1 second. The airway responsiveness was assessed by the reaction to methacholine. The cumulative dose of methacholine that produced a 20% decrease in forced expiratory volume in 1 second was used to measure airway responsiveness. Five subjects who received no prednisone treatment developed a late or dual asthmatic reaction. The albumin concn and total number of cells increased in subjects that were given no prednisone compared to controls. There was a significant increase in the number of neutrophils and a small increase in eosinophilia. There was no significant difference in the counts of other cell types. Results suggest that **toluene** diisocyanate induce late asthmatic reactions causing airway inflammation and that prednisone inhibits these reactions.
[Boschetto P et al; J Allergy Clin Immunol 80 (3):261-267 (1987)]**PEER REVIEWED**

Two men were exposed to **toluene** diisocyanate atmospheres at three different air concn (ca 25, 50 and 70 ug/cu m). The **toluene** diisocyanate atmospheres were generated by a gas-phase permeation method, and the exposures were performed in an 8-cu m stainless-steel test chamber. The effective exposure

period was 4 hr. The isomeric composition of the air in the test chamber was 30% 2,4-**toluene** diisocyanate and 70% 2,6-**toluene** diisocyanate. The concn of **toluene** diisocyanate in air of the test chamber was determined by an HPLC method using the 9-(N-methyl-amino-methyl)-anthracene reagent and by a continuous-monitoring filter-tape instrument. Following the hydrolysis of plasma and urine, the related amines, 2,4-toluenediamine and 2,6-toluenediamine, were determined as pentafluoropropionic anhydride derivatives by capillary gas chromatography using selected ion monitoring in the electron impact mode. In plasma, 2,4- and 2,6-toluenediamine showed a rapid-phase elimination half-time of ca 2-5 hr, and that for the slow phase was greater than 6 days. A connection was observed between concn of 2,4- and 2,6-**toluene** diisocyanate in air and the levels of 2,4- and 2,6-toluenediamine in plasma. The cumulated amount of 2,4-toluenediamine excreted in the urine over 24 hr was ca 15%-19% of the estimated inhaled dose of 2,4-**toluene** diisocyanate, and that of 2,6-toluenediamine was ca 17%-23% of the inhaled dose of 2,6-**toluene** diisocyanate. A connection was found between the cumulated (24 hr) urinary excretion of 2,4- and 2,6-toluenediamine and the air concn of 2,4- and 2,6-**toluene** diisocyanate in the test chamber.
[Brorson T et al; Int Arch Occup Environ Health 63 (4): 253-9 (1991)]**PEER REVIEWED**

Thirty factory workers whose annual exposure to **toluene** diisocyanate amounted to 280 hr were examined. Seven of them had been removed from their jobs for presenting respiratory symptomatology and a further five were removed for presenting bronchial asthma. Their medical histories were consulted and further measures were taken such as a radiological thorax study, total immunoglobulin-E, **toluene** diisocyanate, diphenylmethane diisocyanate and hexamethylene diisocyanate RAST, a basal spirometric study and finally a provocation test. The Rast proved negative in every case. In the spirometric study carried out on the provocation test, four cases showed a significant decrease in the forced expiratory volume in 1 second over 20% and over 40% in the FMEF and PEFR. There was no connection between the four patients who presented an elevated total immunoglobulin-E and the four who presented a positive provocation test. The provocation test proved negative in five of the seven patients removed from their places of work. Two of the four workers who responded positively to the provocation test remained in their places of work during the **toluene** diisocyanate foam test without showing any symptoms. The patients who presented symptoms did not appear to present bronchial obstruction during the provocation test. Nonetheless, patients who seemingly had not shown any symptoms presented what appeared to be bronchial obstruction.
[Duce F et al; Allergol Immunopathol (Madr) 16 (3): 139-44 (1988)]**PEER REVIEWED**

The nature of neurohumoral regulation was studied in 125 healthy workers, aged 20-40 yr, with different length of service and **toluene** diisocyanate exposure levels. Adrenal gland activity and some haematological parameters were determined. Neurohumoral regulation of adaptation processes in **toluene** diisocyanate exposed persons seemed to display some cyclicity, somehow related to the length of service. Two early regulatory phases (service up to 3 yr) had common features unrelated to the exposure levels, while after 3 yr of employment some dissimilarities evolved which did depend on the **toluene** diisocyanate exposure levels.
[Ermakova GA, Kryzanovskaja NA; Gigiena truda i Professional'nye Zabolevanija (7): 22-35 (1988)]**PEER REVIEWED**

Sensitized subjects may develop symptoms of asthma after exposure to isocyanates in their place of work. After challenge with isocyanates in the laboratory, sensitized subjects develop immediate, late and

dual asthmatic reactions. **Toluene** diisocyanate might cause late asthmatic reactions and increase bronchial responsiveness by causing an acute inflammatory reaction in the airways, and that airway inflammation may be responsible for persistence of occupational asthma induced by isocyanates. To test these hypotheses, sensitized subjects were examined during asthmatic reactions induced by exposure to **toluene** diisocyanate in the laboratory. It was observed that late and dual, but not early, asthmatic reactions are associated with a transient increase of bronchial responsiveness which is associated with an acute inflammatory reaction of the airways characterized by an increase of neutrophils followed by eosinophils, by an increase of leukotriene B4 and albumin in bronchoalveolar lavage fluid, and that all these effects are inhibited by steroids. Longitudinal studies suggest that the majority of subjects with occupational asthma continue to have persistent asthma months and yrs after the cessation of exposure, and the results of our studies combined with the results of studies performed by others suggest that the persistence of asthma may be related to the persistence of airway inflammation.
[Fabbri LM et al; Eur Respir J (Suppl 13): 136-38 (1991)]**PEER REVIEWED**

A shortened protocol was developed for the epidemiological measurement of bronchial responsiveness to methacholine without compromising sensitivity, power, precision or safety, and without distorting the numerical value of the PD20.FEV1 (the cumulative dose from a doubling incremental sequence which provokes a 20% decrement in forced expiratory volume in 1 second). It was used in a survey of 254 polyurethane workers (83% of the eligible workforce) exposed occupationally to **toluene** diisocyanate. The mean duration of each test proved to be 38 min, it was well tolerated and 64 workers (25%) proved to be reactors. PD20.FEV1 appeared to be distributed unimodally. It was significantly correlated with questionnaire records of shortness of breath, chest tightness, and wheeze; and with pre-shift forced expiratory volume in 1 second and FEF25-75. Even the reactors requiring the highest dose of 640 cumulative inhalation units (1 unit = one 8.9 ul inhalation of methacholine 1 mg/ml) to generate a PD20 measurement reported significantly more wheeze than the non-reactors. This indicates that the test had clinical meaning throughout its dose range of 0.3-640 units. No correlation was found between PD20 and individual changes in ventilatory function across the working shift, but mean shift changes were negligible and not statistically significant. PD20 was also found to be unrelated to age, sex, race, smoking, cough and atopy.
[Hendrick DJ; Bull Eur Physiopathol Respir 23 (6): 555-9 (1987)]**PEER REVIEWED**

Among the painters handling polyurethane varnish in two furniture manufacturing factories with high **toluene** diisocyanate exposure (0.79 mg/cu m and 0.31 mg/cu m), 26.3% and 15% subjects, respectively displayed asthmatic symptoms, lung function loss, and an increment in mast cell degranulation percentage specific to **toluene** diisocyanate. Some cases of **toluene** diisocyanate linked contact dermatitis were also found among them, being elucidated by positive patch testing to **toluene** diisocyanate. However, the previous abnormalities could not be verified among the painters from another factory with **toluene** diisocyanate concn below the TLV of it (0.11 mg/cu m). It was concluded that both pulmonary hypersensitivity and contact sensitization to **toluene** diisocyanate had occurred in some of the painters included in this study, and that the immunologic effects of **toluene** diisocyanate was concn dependent.
[Huang J et al; Arch Environ Contam Toxicol 21 (4): 607-11 (1991)]**PEER REVIEWED**

The importance of airways inflammation for the development of bronchial hyperresponsiveness and for

exacerbation of asthma was investigated in subjects with occupational asthma. Subjects sensitized to isocyanates, a small molecular weight compound that causes occupational asthma were examined. Studies in asthmatic subjects sensitized to **toluene** diisocyanate demonstrated that late, but not early, asthmatic reactions induced by **toluene** diisocyanate were associated with an acute increase in bronchial responsiveness, and with a marked infiltration of neutrophils and a slight infiltration of eosinophils into the airways, both prevented by steroids. As the late asthmatic reactions and the increase in responsiveness induced by **toluene** diisocyanate were prevented by steroids, but not by indomethacin, it was speculated that cell membrane phospholipid metabolites, which are inhibited by steroids but not by indomethacin, may be involved in **toluene** diisocyanate induced hyperresponsiveness. The results of these studies suggest that bronchial hyperresponsiveness and exacerbation of asthma may be related to inflammation of the airways and that cell membrane phospholipid metabolites may be involved.
[Mapp CE et al; Bull Eur Physiopathol Respir 23 (6): 583-6 (1987)]**PEER REVIEWED**

A study of individuals with occupational asthma induced by **toluene** diisocyanate was conducted. This was a followup of 35 patients, 25 males, with a history of isocyanate sensitization. They had 3 to 41 years' occupational exposure to isocyanate compounds. The subjects had been diagnosed with isocyanate asthma on the basis of their response to bronchial challenge with **toluene** diisocyanate. They were examined an average of 11 mo after diagnosis. They underwent bronchial challenge with **toluene** diisocyanate and methacholine. Forced expiratory volumes in 1 second were measured. Symptoms reported by the subjects were recorded. Twenty seven subjects were still asthmatic at followup as shown by a positive reaction to **toluene** diisocyanate challenge. They showed a deterioration in their forced expiratory volumes in 1 second and response to methacholine similar to that seen at diagnosis. Seventy seven percent of these subjects continued to have recurring attacks of dyspnea, wheezing, and cough which required medication. Twenty two of the asthma subjects had been removed from exposure. Subjects who recovered (did not react to **toluene** diisocyanate at the followup examination) showed an improvement in their forced expiratory volumes in 1 second and a reduced response to methacholine. At the time of diagnosis they tended to have an immediate or dual asthmatic reaction and were younger than the other subjects. The asthmatic subjects had dual or late reactions at diagnosis. It was concluded that respiratory symptoms, isocyanate sensitization, and airway hyperresponsiveness may persist for some time after exposure to **toluene** diisocyanate has ended.
[Mapp CE et al; Am Rev Respir Dis 137 (6): 1326-9 (1988)]**PEER REVIEWED**

Six workers with occupational asthma due to **toluene** diisocyanate were studied. For each worker a detailed clinical and occupational history was taken, and lung function measurement and skin intradermal tests for common allergens were carried out. Methacholine inhalation challenge was performed before **toluene** diisocyanate inhalation, and 8 hr after **toluene** diisocyanate inhalation. Methacholine challenge was within normal limits when performed before **toluene** diisocyanate inhalation, but went into the asthmatic range after **toluene** diisocyanate inhalation. These cases provid evidence that asthma can be induced by **toluene** diisocyanate in the absence of airway hyperresponsiveness. They further demonstrate that an isolated negative methacholine inhalation test cannot be used to exclude sensitization to **toluene** diisocyanate. Screening and follow-up studies on workers exposed on **toluene** diisocyanate require serial measurements of airway responsiveness and of variable air-flow obstruction.
[Mapp CE et al; Eur J Respir Dis 68 (2): 89-95 (1986)]**PEER REVIEWED**

The clinical findings and the results of inhalation challenge with **toluene** diisocyanate and methacholine in 113 subjects with a history of exposure to **toluene** diisocyanate and work-related respiratory symptoms are reported. Only some of the subjects (40.7%) had isocyanate asthma, diagnosed by a positive **toluene** diisocyanate inhalation challenge. Most reactors had a dual (30.4%) or a late (41.3%) response. The interval between the last occupational exposure and the specific challenge was significantly shorter in reactors, and among this group the number of immediate reactions to **toluene** diisocyanate decr progressively with an incr interval. The reactors had a significantly higher proportion of positive responses to methacholine and a significantly lower mean PD[1][5] FEV[1] (provocative dose of methacholine which provoked a 15% decrease in forced expiratory volume in 1 second): reactors 557:g, SEM 92.3; non-reactors 1346:g, SEM 128, P < .01. Methacholine challenge could not identify subjects with isocyanate asthma.
[Moscato G et al; J Occup Med 33 (6): 720-5 (1991)]**PEER REVIEWED**

Toluene diisocyanate is commonly used as the 2,4 and 2,6 isomers. NIOSH has estimated that 50,000 to 100,000 workers in the United States are regularly exposed to diisocyanates. As of 1977, 49,996 were estimated to be exposed to **toluene** diisocyanate alone. Methods for measuring diisocyanate exposures were considered. The current American Conference of Governmental Industrial Hygienists' recommended standard is 0.005 ppm time weighted average and 0.02 ppm peak for four 15 min periods a day. Results of exposure measurements taken in industry were summarized. Health effects of diisocyanates were discussed. In laboratory animals, **toluene** diisocyanate has caused inflammation and necrosis when applied directly to the skin, conjunctivitis when applied to the eyes, and rhinitis, laryngitis, tracheitis, bronchitis, and pneumonia when inhaled. Diisocyanates are potent pulmonary sensitizers capable of causing isocyanate asthma in humans. They can induce nonspecific airways disease and hypersensitivity pneumonitis after either acute or chronic exposure.
[Musk AW et al; Am J Ind Med 13 (3): 331-49 (1988)]**PEER REVIEWED**

A 46 yr old man who had worked in a paint processing plast for over 29 yr was admitted to our hospital with complaints of nocturnal dyspnea and dry cough. A chest X-ray film showed diffuse granular shadows in bilateral lungs. Pulmonary function tests revealed reduction of diffusing capacity and restrictive impairments. Hypersensitivity pneumonitis due to isocyanates was speculated from his occupational history and clinical course. Positive skin tests against **toluene** diisocyanate-human serum albumin and diphenylmethane diisocyanate-human serum albumin, precipitating antibody against **toluene** diisocyanate-human serum albumin, and negative lymphocyte stimulating tests of peripheral blood and bronchoalveolar lavage fluid were also noticed. Environmental provocation test was positive. Histological findings of transbronchial lung biopsy specimens showed diffuse alveolitis and Masson body, but no granulomas. According to these results, the patient was diagnosed as hypersensitivity pneumonitis due to **toluene** diisocyanate. Type III allergy of Gell-Coombs seems to participate in this case. The granulomatous lesion is seen less frequently in isocyanate related hypersensitivity pneumonitis than in hypersensitivity pneumonitis induced by organic dusts, which suggests the difference in immunological and histological reactions between both types of hypersensitivity pneumonitis.
[Nozawa S et al; Nippon Kyobu Shikkan Gakkai Zasshi 27 (11): 1335-41 (1989)]**PEER REVIEWED**

Pulmonary function tests were done and compared to current and past potential exposure levels of **toluene** diisocyanate for 57 **toluene** diisocyanate manufacturing workers and 89 workers not exposed to **toluene** diisocyanate or other known respiratory hazards. The average **toluene** diisocyanate plant experience was 4.1 yr (standard deviation = 2.8). Routine industrial hygiene measurements have shown

toluene diisocyanate exposure below a time-weighted average of 0.005 ppm and a short-term exposure level of 0.02 ppm. A certified industrial hygienist ranked department and job classification by level of potential exposure to **toluene** diisocyanate (none, low, moderate, and high). A questionnaire was administered to determine the prevalence of respiratory symptoms and smoking habits. Using backward regression analysis, cumulative pack-years of cigarette smoking and prevalence of lower respiratory symptoms were statistically significant predictors of a standardized forced expiratory volume at 1 second; however, **toluene** diisocyanate exposure, whether classified as current, highest career level, cumulative, or cumulative highest-to-date, was not associated with a decline in forced expiratory volume.
[Olsen GW et al; J Occup Med 31 (8): 664-7 (1989)]**PEER REVIEWED**

Fifty seven polyurethane foam manufacturing workers and 24 reference workers were followed for 4 yr to clarify the effects on pulmonary function of working in polyurethane foam factories with exposure to **toluene** diisocyanate. No significant differences in the average annual losses of pulmonary function for 4 yr were observed among the 28 polyurethane foam workers whose **toluene** diisocyanate exposure levels were very low (mean = 0.1 ppb, group L), the remaining 29 polyurethane foam workers with mean **toluene** diisocyanate exposure of 5.7 ppb (group H), and the reference workers. However, 15 polyurethane foam workers in group H who had experienced peak exposure excursions to 30 ppb or above with a mean concn of 8.2 ppb showed significantly larger average annual losses in percentage maximal mid-expiratory flow, forced expiratory volume in 1 sec ratio to vital capacity, and forced expiratory flow at 25% of forced vital capacity than expected, and significantly larger average annual losses in some obstructive pulmonary function indices than those of the 14 remaining polyurethane foam workers in group H whose peak exposure excursion levels were 3-14 ppb with a mean time-weighted average of 1.7 ppb, group L, and the reference workers. These findings suggest that the peak exposure excursion level of **toluene** diisocyanate might be important in inducing obstructive pulmonary function changes in the polyurethane foam workers rather than the TWA exposure levels, though further comparative studies of the AAL in those who are exposed to different peak exposure excursion levels but the same mean exposure levels are necessary. From the standpoint of prevention, the proposition that peak exposure excursion levels exceeding 20 ppb should be avoided is reasonable.
[Omae K et al; Int Arch Occup Environ Health 63 (8): 565-9 (1992)]**PEER REVIEWED**

To evaluate the morphologic basis of the different outcomes of **toluene** diisocyanate asthma after quitting occupational exposure, ten patients with **toluene** diisocyanate asthma were examined who showed, at diagnosis, a positive **toluene** diisocyanate challenge test and nonspecific bronchial hyperresponsiveness to methacholine. After diagnosis, all patients ceased work and a 4 to 40 mo follow-up was obtained with three to eight determinations of the cumulative dose producing a 15% fall in forced expiratory volume in 1 second to methacholine in each patient. Bronchoalveolar lavage and biopsy of bronchial muscosa were performed 3 to 39 mo after cessation of work, in the absence of acute exacerbations of the disease. Total cell count in bronchoalveolar lavage fluid was moderately increased in four of ten patients, eosinophils were increased in five of ten patients, and neutrophils were increased in eight of ten patients. Mucosal biopsy specimens of main or lobar bronchi were available in eight of ten patients; epithelial damage and thickening of basement membrane was observed in almost all patients, as well as a mild to moderate inflammatory reaction in the submucosa, mainly represented by lymphocytes, eosinophils, and neutrophils. No relationship was observed between the cellularity of bronchoalveolar lavage and the degree of nonspecific bronchial hyperresponsiveness at the time of bronchoalveolar lavage; mean values of total cells and differential count were not different between patients with

presence or absence of the different histologic findings. Mucosal biopsy and bronchoalveolar lavage were performed also in four subjects exposed to dusts without respiratory symptoms or nonspecific bronchial hyperresponsiveness; similar findings were obtained except for the absence of eosinophils in bronchoalveolar lavage and a lesser degree of basement membrane thickening and inflammatory reaction in the submucosa. The study of the changes in nonspecific bronchial hyperresponsiveness after quitting exposure showed that five of ten patients had a significant improvement in nonspecific bronchial hyperresponsiveness to methacholine, as evaluated by a positive significant linear regression between months of work cessation and forced expiratory volume in 1 sec of methacholine; only one of these five patients had an increased number of eosinophils in bronchoalveolar lavage fluid. By contrast, four of the five patients with persistent nonspecific bronchial hyperresponsiveness after quitting exposure had an increased number of eosinophil in bronchoalveolar lavage. It is suggested that persistent nonspecific bronchial hyperresponsiveness in **toluene** diisocyanate asthma after cessation of work may be related to an inflammatory reaction in which eosinophil infiltration seems to be a major determinant.
[Paggiaro P et al; Chest 98 (3): 536-42 (1990)]**PEER REVIEWED**

The effect of cessation of exposure to **toluene** diisocyanate was studied in six patients with **toluene** diisocyanate induced asthma, proved by a positive inhalation challenge with **toluene** diisocyanate. Bronchial challenges with **toluene** diisocyanate and methacholine were performed, and lobar bronchial biopsies were taken at diagnosis and 6 mo later, after cessation of exposure. Biopsies from four nonasthmatic control subjects were also examined. At diagnosis, asthmatic subjects had thickened reticular basement membrane ($p < 0.05$) and increased numbers of mononuclear cells ($p < 0.05$) and eosinophils ($p < 0.05$) in the lamina propria when compared with control subjects. Electron microscopy showed degranulation of eosinophils and mast cells in asthmatics. Six months after cessation of exposure, the thickness of reticular basement membrane was significantly reduced compared with that at diagnosis ($p < 0.05$), and it decr to values similar to those of control biopsies. Inflammatory cell numbers in bronchial mucosa of asthmatic subjects did not change significantly 6 mo after removal from exposure, and degranulation of eosinophils and mast cells was still present. At the end of the study, airwa hyperresponsiveness to methacholine and/or sensitivity to **toluene** diisocyanate persisted in most of the asthmatic patients despite the cessation of exposure and the disappearance of asthmatic symptoms. In conclusion, in patients with occupational asthma induced by **toluene** diisocyanate, the avoidance of exposure to the sensitizing agent for 6 mo is able to reverse the reticular basement membrane thickening in the bronchial mucosa, but th inflammatory cell infiltrate, the specific sensitivity to **toluene** diisocyanate, and the nonspecific airway hyperreactivity may persist.
[Saetta M et al; Am Rev Respir Dis 145 (1): 169-74 (1992)]**PEER REVIEWED**

Forty-three workers exposed to low levels of **toluene** diisocyanate during the process of producing polyurethane forms were examined immunologically for immunoglobulin-G, A, M, and E and serum enzyme activities such as serum angiotensin converting enzyme, serum lysozyme and glycylproline dipeptidyl aminopeptidase. Air concn of **toluene** diisocyanate was annually measured in various places of work during the past five years from 1979 to 1983. The results obtained in the present study were as follows. The air concn of **toluene** diisocyanate at all places of work was below the permissible concn level of 0.02 ppm throughout the study period. Subjective symptoms and abnormal findings on chest X-ray considered directly related to **toluene** diisocyanate exposure were no observed. No remarkable abnormal findings in blood cell counts and in serum biochemical studies could be seen in any of the workers. The serum immunoglobulin-G levels in workers directly exposed to **toluene** diisocyanate were

significantly higher ($p < 0.05$) than those in workers indirectly exposed to **toluene** diisocyanate and in non-exposed workers. In the study of serum enzymatic activity, serum lysozyme activity in workers exposed directly to **toluene** diisocyanate was significantly higher ($p < 0.01$) than those in workers indirectly exposed to **toluene** diisocyanate and in non-exposed workers.
[Taniwaki H et al; Sangyo Igaku 29 (2): 130-5 (1987)]**PEER REVIEWED**

A case of building related health complaints was investigated with respect to the relationship among frequency of symptoms, antibodies to albumin conjugates of formaldehyde, **toluene** diisocyanate, and trimellitic anhydride, and volatile organic chemicals. The indoor air concn of volatile organic chemicals, formaldehyde, **toluene** diisocyanate and trimellitic anhydride did not exceed Fed-OSHA and ACGIH permissible standards. However, formaldehyde concn ranged between 0.05 and 0.08 ppm. The reported symptoms were multiple, involving the eyes, nose, sinuses, throat, lungs, skeletomuscular system and central nervous system. Anti-formaldehyde, **toluene** diisocyanate, and trimellitic anhydride isotypes were found in 12 of 14 full-time employees and were nondetectable in one part-time employee. The data suggest that a synergistic immunological response to airborne chemicals may be occurring in these subjects. In conclusion, immunological monitoring of affected individuals where chemicals are suspected may prove to be useful in future investigations of building related illness.
[Thrasher JD et al; Am J Ind Med 15 (2): 187-95 (1989)]**PEER REVIEWED**

Diisocyanate inhalation tests (maximal concn, 20 ppb; exposure time, 1-2 hr) were performed using **toluene** diisocyanate (TDI, n = 15) and diphenylmethane diisocyanate (MDI, n = 7) as well as methacholine challenges in 19 workers who had a clinical history of **toluene** diisocyanate/diphenylmethane diisocyanate induced asthma. Additionally volunteers were tested who had n previous contact with diisocyanates: 10 healthy individuals with a negative methacholine test and 14 patients with asthma and a positive methacholine test were exposed to **toluene** diisocyanate. In all, 1 of the normal volunteers and 3 of the patients with asthma unrelated to diisocyanates showed a positive airway reaction to **toluene** diisocyanate, and 13 of the 19 diisocyanate workers displayed a positive result in the **toluene** diisocyanate/diphenylmethane diisocyanate inhalation test; however, only 6 of these 13 individuals reacted to methacholine. Furthermore, 3 of the 6 patients with a negative **toluene** diisocyanate/diphenylmethane diisocyanate challenge test demonstrated a significant response to methacholine. It was concluded that bronchial hyperreactivity as evaluated by the methacholine challenge test is not closely related to isocyanate induced bronchoconstriction and, therefore, the metacholine challenge is only of limited diagnostic value in patients with suspected isocyanate induced asthma.
[Vogelmeier C et al; Int Arch Occup Environ Health 63 (1): 9-13 (1991)]**PEER REVIEWED**

An outbreak of occupational asthma due to **toluene** diisocyanate among industrial workers was described. Four employees at a velcro/like tape manufacturing factory in Taipei, Taiwan were seen in an outpatient clinic complaining of cough, shortness of breath, and wheezing. The symptoms became worse at night and improved after long holidays. The patients' job involved applying an adhesive to the tape. Thirty eight of 45 employees were interviewed by questionnaire and given pulmonary function tests. The pulmonary function tests were given during a workday, after a 10 day holiday, and 5 mo after control measures such as process isolation, improved ventilation, and substitution for **toluene** diisocyanate were instituted. Industrial hygiene sampling for **toluene** diisocyanate was conducted. Fourteen workers had symptoms of asthma or asthmatic bronchitis. The highest attack rate occurred in workers employed in the

tape processing area where the adhesive was applied. Workers in the tape processing area also showed the greatest decr in 1 second forced expiratory volume and forced vital capacity over the workday. Mean **toluene** diisocyanate concn ranged from 0.012 to 0.047 ppm, the highest occurring in the tape processing area and the lowest in the weaving area. The prevalence of asthmatic symptoms was significantly correlated with **toluene** diisocyanate concn. The forced expiratory volume in 1 second and forced vital capacity values were significantly improved after the 10 day holiday and 5 mo after the control methods were instituted. No asthmatic symptoms were reported after 5 mo. It was concluded that **toluene** diisocyanate was responsible for the outbreak and improving the work environment was effective in reducing exposure to **toluene** diisocyanate.
[Wang JD et al; Am J Ind Med 14 (1): 73-8 (1988)]**PEER REVIEWED**

A 41 yr old automobile paint sprayer showed the clinical features of hypersensitivity pneumonitis 1 wk after he had begun to work with paint materials containing **toluene** diisocyanate. His symptoms began 6 to 8 hr after exposure to the agent and spontaneously disappeared by the next morning. He had diffuse, fine reticulonodular shadows on a chest roentgenogram and a restrictive impairment of pulmonary function. Immunoglobulin G antibody to **toluene** diisocyanate-human serum albumin was present in bronchoalveolar lavage fluid and sera: IgA antibody was present only in bronchoalveolar lavage fluid. Also, the patient had sensitized bronchoalveolar lymphocytes to **toluene** diisocyanate-human serum albumin. The histologic findings suggested hypersensitivity pneumonitis. The results of bronchoalveolar lavage, which was repeated on four separate occasions, showed lymphocytosis and a predominance of suppressor cytotoxic T cells. The findings from serial determinations of humoral antibodies showed no changes consistent with the results of clinical and laboratory studies. In contrast, blastogenic responses of bronchoalveolar lymphocytes to **toluene** diisocyanate markedly decr, and the patient showed clinical improvement despite continued exposure to the agent.
[Yoshizawa Y et al; Ann Intern Med 110 (1): 31-4 (1989)]**PEER REVIEWED**

Skin, Eye and Respiratory Irritations:

AS A VAPOR ... /**TOLUENE** DIISOCYANATE/ IS A POWERFUL IRRITANT TO EYES, SKIN, RESPIRATORY TRACT.
[Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984.,p. II-414]**PEER REVIEWED**

Medical Surveillance:

A SCREENING PROGRAM WAS UNDERTAKEN AT A RESEARCH & DEVELOPMENT FACILITY OF A LARGE **TOLUENE**-DIISOCYANATE (TDI) MANUFACTURING CORPORATION. THE PURPOSE WAS TO DETERMINE THE OCCURRENCE OF ANTIBODIES TO TDI IN SELECTED WORKER POPULATIONS. NO TOLYL-REACTIVE IMMUNOGLOBULIN-E ANTIBODIES WERE DETECTED IN SERA WHEN WORKERS WERE EXPOSED ONLY TO AMBIENT TDI CONCN. WORKERS HAD ACUTE EXPOSURES TO TDI AS A RESULT OF SPILLS OR SPLASHES. ANTIBODY RESPONSES DEVELOPED IN 3 OF 4 INDIVIDUALS WHOSE ACUTE EXPOSURES WERE ACCOMPANIED BY IMMEDIATE RESPIRATORY SYMPTOMATOLOGY & A DECREASED FORCED EXPIRATORY VOLUME. AN ANTIBODY RESPONSE DEVELOPED IN 1 OF 9 WORKERS & IMMEDIATE RESPIRATORY

SYMPTOMS, BUT NO SPIROMETRIC CHANGES UPON ACUTE TDI EXPOSURE. ROUTINE SEROLOGIC SCREENING OF WORKERS FOR TOLYL-REACTIVE ANTIBODIES MAY BE OF VALUE IN CONFIRMING SUSPECTED ISOCYANATE EXPOSURE & IN PROVIDING AN EARLY WARNING OF DEVELOPING TDI HYPERSENSITIVITY.
[KAROL MH; J OCCUP MED 23 (11): 741 (1981)]**PEER REVIEWED**

MEDICAL EVALUATIONS OF 15 WORKERS WERE MADE TO DETERMINE THE HEALTH EFFECTS OF EXPOSURE TO TDI, PHOSGENE & TDA. THE FOLLOWING STEPS WERE RECOMMENDED: THE ENTIRE FACTORY POPULATION SHOULD BE SURVEYED PERIODICALLY FOR SYMPTOMS OF LOWER RESPIRATORY TRACT DISEASES & LUNG FUNCTION ABNORMALITIES THAT MAY BE CAUSED BY CHEMICAL EXPOSURE; TDI EXPOSURE SHOULD BE ENDED FOR SENSITIZED WORKERS OR FOR THOSE WITH EXCESSIVE DECLINE IN LUNG FUNCTION.
[COSTELLO RJ, PETERS JM; HEALTH HAZARD EVALUATION DETERMINATION REPORT NO HE-78-31-623, OLIN CORPORATION, ASHTABULA, OHIO 44004; REPORT NIOSH-HE-78-31-623, ORDER NO PB80-195274 (1979)]**PEER REVIEWED**

/Protect/ from exposure those individuals with diseases of blood and liver. Physical exam of exposed personnel annually, incl blood count and liver functions. /**Toluene**-2,4-diisocyanate/
[ITII. Toxic and Hazardous Industrial Chemicals Safety Manual. Tokyo, Japan: The International Technical Information Institute, 1988. 528]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": Whenever medical surveillance is indicated, in particular when exposure to a carcinogen has occurred, ad hoc decisions should be taken concerning ... /cytogenetic and/or other/ tests that might become useful or mandatory. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 23]**PEER REVIEWED**

Comprehensive preplacement medical examinations should be given to each employee. The examination should include a pulmonary function test including FEV1, FVC, and FEV1/FVC, a history of diisocyanate exposure, smoking history, and history of respiratory conditions. The medical data obtained in the pre-placement examination can be used as a base line for periodic examination. Periodic examinations may be useful in detecting a reduction in lung function. Lung function tests, pulmonary history, and pulmonary physical exam should be repeated at least annually. All medical records, including pulmonary function and related medical tests, should be maintained for 30 years.
[Zenz, C. Occupational Medicine-Principles and Practical Applications. 2nd ed. St. Louis, MO: Mosby-Yearbook, Inc, 1988. 1019]**PEER REVIEWED**

Probable Routes of Human Exposure:

Exposure to **toluene** diisocyanate is primarily occupational via inhalation or dermal contact with the aerosol or vapor. Workers may also be exposed through skin contact with freshly cured foam or as a result of spills or splashes. (SRC)

PEER REVIEWED

THE RESPIRATORY HEALTH OF 277 WORKERS IN A NEW **TOLUENE** DIISOCYANATE (TDI) MANUFACTURING PLANT WAS STUDIED PROSPECTIVELY DURING 5 YR OF EXPOSURE. PERSONAL TDI MONITORS WERE USED TO CONTINUOUSLY MEASURE PEAK & 8-HR TIME-WEIGHTED AVG (TWA) CONCN IN MORE THAN 2000 SAMPLES. REGRESSION OF ANNUAL CHANGE ON SMOKING (PACK-YEARS), ATOPIC STATUS & CUMULATIVE TDI EXPOSURE, DICHOTOMIZED AT 68.2 PPB MONTHS INTO LOW & HIGH EXPOSURE GROUPS, SHOWED SIGNIFICANT EFFECTS OF SMOKING ON SPIROMETRIC TESTS & LUNG VOLUMES. AFTER ADJUSTING FOR PACK-YEARS OF SMOKING, THE 74 MEN IN THE HIGH CUMULATIVE TDI EXPOSURE CATEGORY HAD SIGNIFICANTLY LARGER DECLINE IN FEV1 (1-S FORCED EXPIRATORY VOLUME), % FEV (% FORCED EXPIRATORY VOLUME) & FEF25-75% (FORCED EXPIRATORY FRACTION FROM 25 TO 75% VITAL CAPACITY) THAN DID THE 149 MEN IN THE LOW CATEGORY. ANNUAL CHANGE IN FEV1 WAS THEN EXAMINED IN 6 SMOKING-EXPOSURE CATEGORIES: IN NEVER-SMOKERS, AVG ANNUAL DECLINE WAS 38 ML/YR GREATER IN THOSE WITH HIGHER CUMULATIVE TDI EXPOSURE.
[DIEM JE ET AL; AM REV RESPIR DIS 126 (3): 420 (1982)]**PEER REVIEWED**

VAPORS OF THESE COMPD INVARIABLY BECOME AIRBORNE IN POLYMERIZATION REACTIONS, ESP SINCE HEAT & GAS ARE EVOLVED. /**TOLUENE** DIISOCYANATES/
[Hamilton, A., and H. L. Hardy. Industrial Toxicology. 3rd ed. Acton, Mass.: Publishing Sciences Group, Inc., 1974. 335]**PEER REVIEWED**

NIOSH (NOHS Survey 1972-1974) has statistically estimated that 29,284 workers are exposed to TDI in the USA(1). NIOSH (NOES Survey 1981-1983) has statistically estimated that 6,044 workers are exposed to TDI in the USA(2). Since the NOES survey excludes exposure to trade name chemicals which may contain the chemical, occupational exposure could be considerably higher(SRC).
[(1) NIOSH; National Occupational Health Survey (1974) (2) NIOSH; National Occupational Exposure Survey (1983)]**PEER REVIEWED**

Concentration medians for 2,4-**toluene** diisocyanate in 2 plants producing flexible polyurethane foam were 0.70 and 0.33 ppb for the mixing and finishing ends, respectively(1). The respective median values for 2,6-TDI were 0.91 and 1.1 ppb. Maximum concentrations of 2,6-TDI exceeded 64 ppb at the finishing end(1).
[(1) Rando RJ et al; Am Ind Hyg Assoc J 45: 199-203 (1984)]**PEER REVIEWED**

In a Finnish study, TDI vapor concentrations ranged from 25-80 ug/cu m for pouring, 14-44 ug/cu m for paper stripping, and 1-8 ug/cu m for cutting(1). Personal monitors measured 9-34 ug/cu m and 5-30 ug/cu m of the 2,4-isomer for pouring and paper stripping, respectively(1). While 2,4-**toluene** diisocyanate constitutes 80% of TDI, and 2,6-**toluene** diisocyanate 20%, the 2,4-isomer is more reactive so that the concentration of the 2,6-isomer is higher in workplace air(1). The percentage of 2,4-**toluene** diisocyanate to total **toluene** diisocyanate measured with the personal monitors ranged from 29 to 69%(1). TDI levels of 1.3-2.8 ppb were detected in air inside a Swedish factory manufacturing polyurethanes(2).

[(1) Rosenberg C, Savolainen H; J Chromatography 367: 385-92 (1986) (2) Audunsson G et al; Intern J Environ Anal Chem 20: 85-100 (1985)]**PEER REVIEWED**

Mean concn ranges of TDI reported in ambient workplace air were 0.7-710 ug/cu m in TDI production, ND - 1490 ug/cu m during polyurethane foam production, 70-140 mg/cu m during elastomer production, 13 - 1050 ug/cu m during polyurethane foam use, 10-710 ug/cu m during polyurethane spray paint use, and <1-740 ug/cu m during the production of polyurethane-coated wire(1). Mean concn in personal samples ranged from ND-540 ug/cu m during polyurethane foam production and 2-1220 ug/cu m during polyurethane spray foam use(1). Additionally, mean concn of TDI released from insulation in a ship's hold was reported to be 120-150 ug/cu m and that released from coated fabric in a workplace 2-10 ug/cu m(1). During the outdoor application of TDI foam to a 40 ft diameter storage tanks, the mean atmospheric TDI concentration downwind from the spray gun was 0.3 ppm at 8 ft, 0.02 ppm at 40 ft, and 0.002 ppm at 150 ft(2). TDI was not detected more than 8 ft upwind of the spray gun(2). Air samples taken within two ft of the foam surface immediately after spraying had ceased was found to be 0.03 ppm(2). Mean TDI concentrations near the pumping equipment during material transfer was 0.02 ppm(2).

[(1) IARC Monograph on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. 39: 287-323 (1985) (2) Peterson JE et al; Amer Id Hyg Assoc J 23: 345-52 (1962)]**PEER REVIEWED**

TOLUENE DIISOCYANATE

CASRN: 26471-62-5

For other data, click on the Table of Contents

Evidence for Carcinogenicity:

No data are available in humans. Sufficient evidence of carcinogenicity in animals. OVERALL EVALUATION: Group 2B: The agent is possibly carcinogenic to humans.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. S7 72 (1987)]**PEER REVIEWED**

TOLUENE DIISOCYANATE

CASRN: 26471-62-5

For other data, click on the Table of Contents

Human Toxicity Excerpts:

TOLUENE DIISOCYANATE (TDI) SENSITIVITY ACCOMPANIED BY NONSPECIFIC BRONCHIAL HYPERRESPONSIVENESS OCCURS IN 5% OF OCCUPATIONALLY EXPOSED WORKERS. THE CASE OF A 32 YR OLD WORKER FOLLOWED LONGITUDINALLY AFTER REMOVAL FROM ISOCYANATE EXPOSURE IS REPORTED. TDI REACTIVITY WAS LOST 11 MONTHS AFTER REMOVAL FROM EXPOSURE & NONSPECIFIC BRONCHIAL HYPERRESPONSIVENESS RESOLVED AFTER 17 MONTHS. IMMUNOPHARMACOLOGIC RESULTS SHOW THAT THE WORKER'S INITIAL DECREASED ABILITY OF LYMPHOCYTES TO PRODUCE CYCLIC-AMP RETURNED TO NEAR NORMAL AFTER 2 YR. IMMUNOGLOBULIN-E ANTIBODIES TO A HUMAN SERUM ALBUMIN TOLYL MONOISOCYANATE CONJUGATE WERE STILL PRESENT THIS TIME.
[BUTCHER BT ET AL; J ALLERGY CLIN IMMUNOL 70 (4): 231 (1982)]**PEER REVIEWED**

ACCIDENTAL SPLASH ... IN EYES OF WORKMEN HAS CAUSED KERATITIS & CONJUNCTIVITIS. ONE CASE ... DESCRIBES "UNUSUAL AMT OF PHOTOPHOBIA & BLEPHAROSPASM" ... SECOND CASE ... INVOLVED SEVERE IRIDOCYCLITIS & SECONDARY GLAUCOMA.
[Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986. 929]**PEER REVIEWED**

WORKERS EXPOSED ... DEVELOPED IRRITATION OF EYES, IRRITATION OR DRYNESS OF THROAT &/OR TIGHTNESS OF CHEST. EXPOSURE TO LEVELS AS LOW AS 0.014 MG/CU M (0.002 PPM) CAN RESULT IN CHRONIC LOSS OF PULMONARY FUNCTION. MORE ACUTE, ASTHMATIC TYPE OF BRONCHITIS IS ... TYPICAL, FRANK ASTHMA MAY OCCUR.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V19 311 (1979)]**PEER REVIEWED**

RESP SYMPTOMS ... IMPROVE ... AFTER REMOVAL FROM /OCCUPATIONAL/ EXPOSURE, BUT ... RE-EXPOSURE TO EVEN MINIMAL CONCN ... PRODUCED RECURRENCE OF ... SYMPTOMS. HYPERSENSITIVITY ... ARISES AFTER ... INHALATION, & IT HAS BEEN RELATED TO IMMUNOLOGICAL CHANGES ... & TO ALTERED BETA-ADRENERGIC FUNCTION.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V19 311 (1979)]**PEER REVIEWED**

... DOSE-RESPONSE RELATIONSHIP OF ACUTE PULMONARY FUNCTION CHANGES AMONG 112 WORKERS EXPOSED ... TO 0.0035-0.06 MG/CU M (0.0005-0.009 PPM). 2-YR FOLLOW-UP EXAM OF 57 OF WORKERS DISCLOSED DECR IN PULMONARY FUNCTION ...

RELATED TO EXPOSURE LEVELS, CONTROLLING FOR AGE, MO EMPLOYED, SMOKING ... & PHYSIQUE.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V19 311 (1979)]**PEER REVIEWED**

A series of workers with exposure to and respiratory symptoms from **toluene** diisocyanate was compared with a group of exposed, asymptomatic workers and with normal controls using immunologic and clinical evaluations. Improved understanding of **toluene** diisocyanate-induced respiratory disease may best be achieved by categorizing the symptomatic workers into at least 3 and possibly 4 groups: immunologic asthma; pre-existing chronic respiratory disease exacerbated or unaffected by **toluene** diisocyanate; asthma coincidental with exposure, and possibly respiratory disease secondary to toxic or inflammatory mechanisms.
[Patterson R et al; Int Arch Allergy Appl Immunol 84 (1): 93-100 (1987)]**PEER REVIEWED**

Subjects exposed to 0.0010 to 0.0015 ppm of **toluene** diisocyanate demonstrated a normal age and smoking-related rate of decline in forced expiratory volume in 1 second and no evidence that it was related to isocyanate exposures.
[Musk AW et al; J Occup Med 27 (12): 917-20 (1985)]**PEER REVIEWED**

Twelve subjects were studied with inhalation challenge testing to **toluene** diisocyanate because of suspected asthma based on a consistent clinical and occupational history. In seven cases, asthma was documented by a positive inhalation challenge to low levels of **toluene** diisocyanate. Six of the seven reactors had persistent respiratory symptoms and required daily treatment even though they had been removed from isocyanate exposure for intervals as long as 12 years (mean 4.5 years). These six reactors had either dual (four cases) or late bronchospasm (two cases) to less than 20 ppb and all had a positive methacholine or cold air challenge prior to study. The one reactor with a negative methacholine challenge had a positive (immediate) bronchospastic response to a challenge performed one week after removal from isocyanate exposure. Five workers had a negative challenge, two of whom had persistent respiratory symptoms and positive methacholine challenges at the time of inhalation testing. ... Respiratory symptoms may persist following long-term removal from occupational exposure to and are associated with nonspecific bronchial hyperreactivity. The sensitivity may also persist for a long time even in the absence of any additional occupational exposure. Long-term prospective studies of symptomatic isocyanate workers are needed to fully define the extent of this problem.
[Moller DR et al; Chest 90 (4): 499 (1986)]**PEER REVIEWED**

Two workers who developed asthmatic symptoms were studied with inhalation provocation tests using ... **toluene** diisocyanate. Subjects did not show asthmatic reations to TDI challenge.
[Mapp CE et al; Ann Allergy 54 (5): 424-9 (1985)]**PEER REVIEWED**

Amine induced asthma was studied in polyurethane foam workers. A total of 12 subjects, occupationally exposed to polyurethane foams, who complained of wheezing and breathlessness at work were tested. Subjects were given 20 to 2000 ug methacholine. Forced expiratory volume in 1 sec was measured. Subjects were challenged with 0.01 ppm **toluene** diisocyanate for 15 min in an atmosphere chamber. Forced expiratory volume in 1 sec was measured. Positive tests were considered as a 15% fall in forced

expiratory volume in 1 sec. High sensitivity to methacholine was seen in ten subjects with a 15% fall in forced expiratory volume in 1 sec at <1000 ug; normal subjects responded at 2000 ug. All subjects reacted to **toluene** diisocyanate.
[Cardura F, Moscata G; Brit J Indus Med 41: 552-3 (1984)]**PEER REVIEWED**

... The toxicity of inhaled vapors of diisocyanates is summarized. Humans are exposed to high concentrations of diisocyanates in polyurethane industries. Toxic symptoms are acute inflammation with lachrymation, rhinitis, soreness and burning in the throat and upper part of the chest, and coughing. Fire fighters are particularly prone to these clinical symptoms. The toxic limit value for **toluene** diisocyanate is 0.005 ppm. Exposure to diisocyanates can cause asthma.
[Davies RJ; Clinics in Immunology and Allergy 4 (1): 103-23 (1984)]**PEER REVIEWED**

The respiratory status of factory workers exposed continously to isocyanates over 10 years was studied. A total of 80 workers in two facilities that manufactured fixtures used in the interiors of cars were examined and underwent spirometry before and after work. Of these, 12 were comparisons not exposed to **toluene** diisocyanate. Subjects included those previously examined in 1971. Ventilatory capacity tests were performed inlcuding forced expiratory volume in 1 sec and forced vital capacity testing. Annual decrements were calculated. The mean average concentration of **toluene** diisocyanate was not more than 0.0033 ppm respectively. Subjects who had been studied previously had a mean forced vital capacity of 104.6% and a mean forced expiratory volume in 1 sec of 107% of predicted values. Three subjects with significant obstruction in the lung function tests were smokers. The comparisons in facility 1 had a significantly lower percentage of the predicted forced fital capacity and forced expiratory volume than the exposed population. Most of the data from 1971 for annual decrement calculations were not reliable. A 10% decrement in forced vital capacity and forced expiratory volume in 1 second was indicative of significant postshift decline and would indicate the presence of isocyanate asthma or hypersensitivity; no subject at either facility met the criteria.
[Gee JB; Morgan WKC; J Occup Med 27 (1): 15-8 (1985)]**PEER REVIEWED**

The mechanism by which late asthmatic reactions are induced by **toluene** diisocyanate, a low molecular weight chemical that causes occupational asthma in exposed subjects, is unknown. An investigation was conducted to determine whether early and late asthmatic reactions induced by **toluene** diisocyanate are associated with changes in airway responsiveness to methacholine and airway inflammation as determined by bronchoalveolar lavage. Forced expiratory volume in 1 second was measured before and at regular intervals after exposure to **toluene** diisocyanate and dose-response curves to methacholine and bronchoalveolar lavage at 8 hr after **toluene** diisocyanate /were performed/ in a group of 6 subjects with late asthmatic reactions and in 6 subjects with only early asthmatic reactions. The same procedure was followed 2 hr after **toluene** diisocyanate in a group of 6 subjects with previously documented late asthmatic reactions and in a group of 6 subjects without any previously documented asthmatic reaction after **toluene** diisocyanate. In subjects with late asthmatic reactions, neutrophils were increased at both 2 hr and 8 hr and eosinophils and airway responsiveness were increased only at 8 hr. By contrast, neutrophils, eosinophils and airway responsiveness were not increased at 8 hr after **toluene** diisocyanate in subjectswith an early asthmatic reaction or at 2 hr after **toluene** diisocyanate in normal control subjects. These results suggest that late asthmatic reactions to **toluene** diisocyanate, and the associated increase in airway responsiveness may be caused by airway inflammation.
[Fabbri LM et al; Am Rev Respir Dis 136 (1): 36-42 (1987)]**PEER

REVIEWED**

Technical grade **toluene** diisocyanate induced chromosome aberrations after a 24 hr treatment in the absence of metabolic activation in human whole blood lymphocyte cultures.
[Maki-Paakkanen J, Norppa H; Toxicol Lett 36 (1): 37-43 (1987)]**PEER REVIEWED**

To determine whether late asthmatic reactions and the associated increase in airway induced by **toluene** diisocyanate are linked to airway inflammation, inhibition by prednisone was investigated. Ten "sensitized" subjects were studied in 2 sets of experiments. In the first set, each subject was given no treatment and was studied before and for 8 hr after exposure to **toluene** diisocyanate. In the second set, 2 to 4 wk later, each subject was studied before treatment and then during treatment with prednisone (50 mg once a day for 3 days, orally), both before and after exposure to **toluene** diisocyanate. To assess late asthmatic reactions to **toluene** diisocyanate FEV1 /was measured/ immediately before and after exposure, then hourly for 8 hr. To assess changes in airway responsiveness, a /measurement was made of/ the provocation dose (mg) of methacholine causing a 20% decrease in FEV1 (PD20FEV1) before and 8 hr after exposure to **toluene** diisocyanate. When the subjects received no prednisione treatment, **toluene** diisocyanate caused late asthmatic reactions and increased airway responsiveness. By contrast, when the subjects received prednisone, **toluene** diisocyanate caused no late asthmatic reaction or increased airway responsiveness. Prednisone did not change baseline airway caliber or airway responsiveness. These results suggest that late asthmatic reactions and the associated increase in airway responsiveness induced by **toluene** diisocyanate in "sensitized" subjects may depend on the development of a steroid-responsive acute inflammatory reaction within the airways.
[Fabbri LM; Am Rev Respir Dis 132 (5): 1010-4 (1985)]**PEER REVIEWED**

Case reports of keratophathy in polyurethane production workers were examined. The experimental production of similar conditions was studied in cats and a monkey. A male polyurethane worker complained of blurred vision which improved over weekends away from work. The only significant finding on examination of the eyes was subepithelial corneal vesicles of 30 to 50 micrometers in diameter. A second patient, a female worker from the same facility, also complained of attacks of blurred vision. Slit lamp examination showed deep or subepithelial vacuolization only in the palpebral aperture. ... Corneas were normal between 3 day and 2 weeks. Exposure to **toluene** diisocyanate did not result in the clinical appearance of the eye resembling that of the workers.
[Potts AM et al; Am J Indust Med 9 (2): 203-13 (1986)]**PEER REVIEWED**

Symptoms and lung function of workers exposed to isocyanates in polyurethane foam factories were studied. A group of 67 workers was examined for **toluene**-diisocyanate ... exposure. Measurements were made by samples obtained from subject carried pumps. Interviews were also conducted for information of symptoms involving the nose, eyes, upper airways, and lung. Another group of 56 nonexposed workers was determined by spirometry and nitrogen wash out prior to the work shift. The exposed workers were examined again immediately after work. The variables studied were forced expired vital capacity and forced expired volume in 1 second. ... The highest exposure group was foaming machine workers, with a day mean exposure of 0.023 mg/cu m. Nonsmokers showed an increased frequency of symptoms involving the nose, throat, and dyspnea. Smokers had no significant increase. Smokers of the exposed group reported coughing. Only smokers reported symptoms classified as chronic bronchitis, with frequency independent of exposure. Decreased forced expired vital capacity and forced expired

volume were observed in the exposed group. This group also showed increased expired vital capacity. Lung function impairment was restricted to smokers. Spirometric and nitrogen washout variables did not change significantly during the work shift. Decreasing spirometric values with increased exposure was seen in smokers. Conclusions indicate that mean exposure of 0.01 mg/cu m/day to isocyanates may give an increased frequency of symptoms in nonsmokers.
[Alexanderson R et al; Internat Archives of Occup Environ Health 55 (2): 149-57 (1985)]**PEER REVIEWED**

A survey of the incidence of occupational asthma in a steel coating factory was conducted. The survey was prompted by two male employees developing symptoms suggestive of occupational asthma. The cohort consisted of 221 males employed in the coating shop. A respiratory questionnaire was administered. Spirometric tests were conducted. Peak expiratory flow rate studies were performed on 50 subjects. Twenty one subjects reported symptoms of occupational asthma. Sixty three had other work related symptoms and 58 had respiratory symptoms unrelated to work. The mean length of employment of the subjects with asthmatic symptoms was 7.7 years. All symptomatic subjects had significantly reduced 1 second forced expiratory volumes, compared to asymptomatic workers. 21% of the peak expiratory flow rates were indicative of work related asthma. Two symptomatic subjects were administered inhalation challenge tests with **toluene** diisocyanate after it was discovered that one of the coatings that had been used for 8 years released **toluene** diisocyanate during the coating process. Both subjects showed decreases in forced expiratory volumes of at least 15% below the baseline values. Environmental sampling for **toluene** diisocyanate indicated concentrations ranging from below 0.001 to 0.026 ppm. The coating containing **toluene** diisocyanate was removed from the process. A follow-up survey conducted 1 year later showed that 17 of the symptomatic subjects had become asymptomatic or improved.
[Venables KM et al; Brit J Indus Med 42 (8): 517-24 (1985)]**PEER REVIEWED**

The presence of different thresholds on bronchial reactivity to **toluene** diisocyanate was tested in 20 spray painters employed in the furniture industry and affected by TDI induced asthma. Bronchial provocation tests failed to demonstrate nonspecific hyperreactivity to methacholine. Exposure of the workers to **toluene** diisocyanate in concentrations ranging from 0.02 to 0.25 ppm demonstrated the occurrence of low, moderate and high thresholds of airways response to **toluene** diisocyanate in nine, seven and four patients, respectively. There was no association between the **toluene** diisocyanate response threshold and the positive response pattern to the lower range of **toluene** diisocyanate levels, but six of the nine patients with low threshold of response to **toluene** diisocyanate and six of the 11 patients with moderate or high thresholds had nonspecific bronchial hyperreactivity. The response to **toluene** diisocyanate also was not associated with the duration of the asthmatic condition, smoking, cessation of work or nonspecific response to methacholine. The pattern of response was not dose dependent in ten of 13 patients who had two positive bronchial provocation tests with different levels of **toluene** diisocyanate, although dual responses were recorded in three patients who had late reactions at low concentrations of **toluene** diisocyanate. The value of forced expiratory volume in one second, recorded during immediate reactions, showed a dose response relationship, in that it declined by 28.4% at lower **toluene** diisocyanate levels as compared to 38.3% following inhalation of higher doses of the compound; no such association was established for the late reaction to **toluene** diisocyanate. The results conclude that patients who are sensitive to **toluene** diisocyanate may have different thresholds of response to the agent.

[Paggiaro PL et al; Respiration 50 (3): 167-73 (1986)]**PEER REVIEWED**

Respiratory variables were measured in workers exposed to **toluene** diisocyanate in Canada. Exposure and effect relationships were studied. Results from 95 isocyanate workers were compared with unexposed workers. Exposed workers were grouped according to production areas based on isocyanate concentrations measured. Individual monitors were worn to identify exposure for some workers. Symptoms and history of respiratory illness were compared through questionnaires. Pulmonary function tests included forced vital capacity, forced expiratory volume in 1 second, and forced expiratory flow at 50% and 75% of vital capacity. Pulmonary function was measured at the beginning and end of work shifts on Monday, Wednesday, and Friday of a work week. Regression analysis of exposure concentration and other variables was attempted. When comparisons were adjusted for smoking habits, exposed workers had a significantly lower family history of respiratory complaints. Isocyanate workers had slightly lower base line lung function than comparisons, but had significantly higher declines in pulmonary function over the work week. A 5% or greater decline over a day occurred in 44 percent of exposed but only 22% of comparison workers. Foam line and finishing area workers had greatest declines in forced vital capacity and forced expiratory volume in 1 second. It was concluded that although regression analysis does not show an exposure/effect relationship, an all or none effect may be operating with acute and chronic compartments. However, sample size may have been insufficient.
[Holness DL et al; J Occup Med 26 (6): 449-55 (1984)]**PEER REVIEWED**

Toluene diisocyanate may produce a true hemorrhagic syndrome affecting the bone marrow and producing primarily thrombocyte series suppression.
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 303]**PEER REVIEWED**

All workers develop eye, nose, and throat irritation at 0.5 ppm. Sensitized individuals may manifest symptoms at levels as low as 0.02 ppm.
[Ellenhorn, M.J. and D.G. Barceloux. Medical Toxicology - Diagnosis and Treatment of Human Poisoning. New York, NY: Elsevier Science Publishing Co., Inc. 1988. 880]**PEER REVIEWED**

A worker developed **toluene** diisocyanate induced asthma in 1974. On reassessment, 11 yr after leaving the chemical plant where **toluene** diisocyanate was produced, he had no respiratory symptoms and normal bronchial reactivity in response to methacholine, and showed no reaction when challenged with a subirritant concn of **toluene** diisocyanate. He developed asthma within five months of returning to the workplace. Repeat challenge testing showed bronchial hyperreactivity to methacholine and to the specific sensitising agent, **toluene** diisocyanate. This clinical pattern could be due to underlying **toluene** diisocyanate sensitivity with resolution and reappearance of hyperresponsiveness to methacholine and **toluene** diisocyanate reactivity associated with workplace **toluene** diisocyanate exposure. Alternatively, this worker may have developed sensitisation to **toluene** diisocyanate anew.
[Banks DE, Rando RJ; Thorax 43 (8): 1988 660-2]**PEER REVIEWED**

An investigation of the persistence of isocyanate induced asthma in workers with negligible occupational exposure was carried out. Six asthmatic workers, proven to be **toluene** diisocyanate sensitive by inhalation challenge testing in a longitudinal study of respiratory health risks associated with

polyurethane foam production, were examined. The subjects were followed for 5 yr during which they completed a respiratory symptom questionnaire annually. Pulmonary function and responsiveness to methacholine challenge were measured annually. **toluene** diisocyanate concn in their breathing zones were measured. After the original survey the six subjects were transferred to areas thought to have negligible **toluene** diisocyanate exposures. None of the subjects had respiratory or asthmatic complaints before they started work in polyurethane production. The respiratory symptoms of the subjects did not improve during the followup period. All six had bronchial hyperresponsiveness to methacholine that did not resolve over time. Three subjects demonstrated deficits in 1 second forced expiratory volume of greater than 15% on one of the testing days during the followup period. The need for less or additional asthma therapy of the subjects could not be predicted. The mean time weighted average **toluene** diisocyanate exposure experienced by the subjects was 0.64 ppb; less than 5% of the OSHA standard of 20 ppb. It was concluded that although the outcome of isocyanate induced asthma cannot be predicted, the asthmatic symptoms of these workers have persisted despite the negligible **toluene** diisocyanate exposures.
[Banks DE et al; Chest 97 (1): 121-5 (1990)]**PEER REVIEWED**

The prevention of airway inflammation caused by **toluene** diisocyanate by prednisone was studied. Healthy **toluene** diisocyanate sensitive individuals were exposed to 0.018 ppm **toluene** diisocyanate in a test chamber. Bronchoalveolar lavage fluid was collected with a flexible fiberoptic bronchoscope. The lavage fluid was spun in a cytocentrifuge and stained with May/Grunwald/Giemsa for differential cell count. The total cell count was performed on resuspended cell pellets. A late asthmatic response was characterized by the occurrence of less than 20% of free expiratory volume in 1 second. The airway responsiveness was assessed by the reaction to methacholine. The cumulative dose of methacholine that produced a 20% decrease in forced expiratory volume in 1 second was used to measure airway responsiveness. Five subjects who received no prednisone treatment developed a late or dual asthmatic reaction. The albumin concn and total number of cells increased in subjects that were given no prednisone compared to controls. There was a significant increase in the number of neutrophils and a small increase in eosinophilia. There was no significant difference in the counts of other cell types. Results suggest that **toluene** diisocyanate induce late asthmatic reactions causing airway inflammation and that prednisone inhibits these reactions.
[Boschetto P et al; J Allergy Clin Immunol 80 (3):261-267 (1987)]**PEER REVIEWED**

Two men were exposed to **toluene** diisocyanate atmospheres at three different air concn (ca 25, 50 and 70 ug/cu m). The **toluene** diisocyanate atmospheres were generated by a gas-phase permeation method, and the exposures were performed in an 8-cu m stainless-steel test chamber. The effective exposure period was 4 hr. The isomeric composition of the air in the test chamber was 30% 2,4-**toluene** diisocyanate and 70% 2,6-**toluene** diisocyanate. The concn of **toluene** diisocyanate in air of the test chamber was determined by an HPLC method using the 9-(N-methyl-amino-methyl)-anthracene reagent and by a continuous-monitoring filter-tape instrument. Following the hydrolysis of plasma and urine, the related amines, 2,4-toluenediamine and 2,6-toluenediamine, were determined as pentafluoropropionic anhydride derivatives by capillary gas chromatography using selected ion monitoring in the electron impact mode. In plasma, 2,4- and 2,6-toluenediamine showed a rapid-phase elimination half-time of ca 2-5 hr, and that for the slow phase was greater than 6 days. A connection was observed between concn of 2,4- and 2,6-**toluene** diisocyanate in air and the levels of 2,4- and 2,6-toluenediamine in plasma. The cumulated amount of 2,4-toluenediamine excreted in the urine over 24 hr was ca 15%-19% of the

estimated inhaled dose of 2,4-**toluene** diisocyanate, and that of 2,6-toluenediamine was ca 17%-23% of the inhaled dose of 2,6-**toluene** diisocyanate. A connection was found between the cumulated (24 hr) urinary excretion of 2,4- and 2,6-toluenediamine and the air concn of 2,4- and 2,6-**toluene** diisocyanate in the test chamber.
[Brorson T et al; Int Arch Occup Environ Health 63 (4): 253-9 (1991)]**PEER REVIEWED**

Thirty factory workers whose annual exposure to **toluene** diisocyanate amounted to 280 hr were examined. Seven of them had been removed from their jobs for presenting respiratory symptomatology and a further five were removed for presenting bronchial asthma. Their medical histories were consulted and further measures were taken such as a radiological thorax study, total immunoglobulin-E, **toluene** diisocyanate, diphenylmethane diisocyanate and hexamethylene diisocyanate RAST, a basal spirometric study and finally a provocation test. The Rast proved negative in every case. In the spirometric study carried out on the provocation test, four cases showed a significant decrease in the forced expiratory volume in 1 second over 20% and over 40% in the FMEF and PEFR. There was no connection between the four patients who presented an elevated total immunoglobulin-E and the four who presented a positive provocation test. The provocation test proved negative in five of the seven patients removed from their places of work. Two of the four workers who responded positively to the provocation test remained in their places of work during the **toluene** diisocyanate foam test without showing any symptoms. The patients who presented symptoms did not appear to present bronchial obstruction during the provocation test. Nonetheless, patients who seemingly had not shown any symptoms presented what appeared to be bronchial obstruction.
[Duce F et al; Allergol Immunopathol (Madr) 16 (3): 139-44 (1988)]**PEER REVIEWED**

The nature of neurohumoral regulation was studied in 125 healthy workers, aged 20-40 yr, with different length of service and **toluene** diisocyanate exposure levels. Adrenal gland activity and some haematological parameters were determined. Neurohumoral regulation of adaptation processes in **toluene** diisocyanate exposed persons seemed to display some cyclicity, somehow related to the length of service. Two early regulatory phases (service up to 3 yr) had common features unrelated to the exposure levels, while after 3 yr of employment some dissimilarities evolved which did depend on the **toluene** diisocyanate exposure levels.
[Ermakova GA, Kryzanovskaja NA; Gigiena truda i Professional'nye Zabolevanija (7): 22-35 (1988)]**PEER REVIEWED**

Sensitized subjects may develop symptoms of asthma after exposure to isocyanates in their place of work. After challenge with isocyanates in the laboratory, sensitized subjects develop immediate, late and dual asthmatic reactions. **Toluene** diisocyanate might cause late asthmatic reactions and increase bronchial responsiveness by causing an acute inflammatory reaction in the airways, and that airway inflammation may be responsible for persistence of occupational asthma induced by isocyanates. To test these hypotheses, sensitized subjects were examined during asthmatic reactions induced by exposure to **toluene** diisocyanate in the laboratory. It was observed that late and dual, but not early, asthmatic reactions are associated with a transient increase of bronchial responsiveness which is associated with an acute inflammatory reaction of the airways characterized by an increase of neutrophils followed by eosinophils, by an increase of leukotriene B4 and albumin in bronchoalveolar lavage fluid, and that all these effects are inhibited by steroids. Longitudinal studies suggest that the majority of subjects with occupational asthma continue to have persistent asthma months and yrs after the cessation of exposure,

and the results of our studies combined with the results of studies performed by others suggest that the persistence of asthma may be related to the persistence of airway inflammation.
[Fabbri LM et al; Eur Respir J (Suppl 13): 136-38 (1991)]**PEER REVIEWED**

A shortened protocol was developed for the epidemiological measurement of bronchial responsiveness to methacholine without compromising sensitivity, power, precision or safety, and without distorting the numerical value of the PD20.FEV1 (the cumulative dose from a doubling incremental sequence which provokes a 20% decrement in forced expiratory volume in 1 second). It was used in a survey of 254 polyurethane workers (83% of the eligible workforce) exposed occupationally to **toluene** diisocyanate. The mean duration of each test proved to be 38 min, it was well tolerated and 64 workers (25%) proved to be reactors. PD20.FEV1 appeared to be distributed unimodally. It was significantly correlated with questionnaire records of shortness of breath, chest tightness, and wheeze; and with pre-shift forced expiratory volume in 1 second and FEF25-75. Even the reactors requiring the highest dose of 640 cumulative inhalation units (1 unit = one 8.9 ul inhalation of methacholine 1 mg/ml) to generate a PD20 measurement reported significantly more wheeze than the non-reactors. This indicates that the test had clinical meaning throughout its dose range of 0.3-640 units. No correlation was found between PD20 and individual changes in ventilatory function across the working shift, but mean shift changes were negligible and not statistically significant. PD20 was also found to be unrelated to age, sex, race, smoking, cough and atopy.
[Hendrick DJ; Bull Eur Physiopathol Respir 23 (6): 555-9 (1987)]**PEER REVIEWED**

Among the painters handling polyurethane varnish in two furniture manufacturing factories with high **toluene** diisocyanate exposure (0.79 mg/cu m and 0.31 mg/cu m), 26.3% and 15% subjects, respectively displayed asthmatic symptoms, lung function loss, and an increment in mast cell degranulation percentage specific to **toluene** diisocyanate. Some cases of **toluene** diisocyanate linked contact dermatitis were also found among them, being elucidated by positive patch testing to **toluene** diisocyanate. However, the previous abnormalities could not be verified among the painters from another factory with **toluene** diisocyanate concn below the TLV of it (0.11 mg/cu m). It was concluded that both pulmonary hypersensitivity and contact sensitization to **toluene** diisocyanate had occurred in some of the painters included in this study, and that the immunologic effects of **toluene** diisocyanate was concn dependent.
[Huang J et al; Arch Environ Contam Toxicol 21 (4): 607-11 (1991)]**PEER REVIEWED**

The importance of airways inflammation for the development of bronchial hyperresponsiveness and for exacerbation of asthma was investigated in subjects with occupational asthma. Subjects sensitized to isocyanates, a small molecular weight compound that causes occupational asthma were examined. Studies in asthmatic subjects sensitized to **toluene** diisocyanate demonstrated that late, but not early, asthmatic reactions induced by **toluene** diisocyanate were associated with an acute increase in bronchial responsiveness, and with a marked infiltration of neutrophils and a slight infiltration of eosinophils into the airways, both prevented by steroids. As the late asthmatic reactions and the increase in responsiveness induced by **toluene** diisocyanate were prevented by steroids, but not by indomethacin, it was speculated that cell membrane phospholipid metabolites, which are inhibited by steroids but not by indomethacin, may be involved in **toluene** diisocyanate induced hyperresponsiveness. The results of these studies suggest that bronchial hyperresponsiveness and exacerbation of asthma may be related to

inflammation of the airways and that cell membrane phospholipid metabolites may be involved.
[Mapp CE et al; Bull Eur Physiopathol Respir 23 (6): 583-6 (1987)]**PEER REVIEWED**

A study of individuals with occupational asthma induced by **toluene** diisocyanate was conducted. This was a followup of 35 patients, 25 males, with a history of isocyanate sensitization. They had 3 to 41 years' occupational exposure to isocyanate compounds. The subjects had been diagnosed with isocyanate asthma on the basis of their response to bronchial challenge with **toluene** diisocyanate. They were examined an average of 11 mo after diagnosis. They underwent bronchial challenge with **toluene** diisocyanate and methacholine. Forced expiratory volumes in 1 second were measured. Symptoms reported by the subjects were recorded. Twenty seven subjects were still asthmatic at followup as shown by a positive reaction to **toluene** diisocyanate challenge. They showed a deterioration in their forced expiratory volumes in 1 second and response to methacholine similar to that seen at diagnosis. Seventy seven percent of these subjects continued to have recurring attacks of dyspnea, wheezing, and cough which required medication. Twenty two of the asthma subjects had been removed from exposure. Subjects who recovered (did not react to **toluene** diisocyanate at the followup examination) showed an improvement in their forced expiratory volumes in 1 second and a reduced response to methacholine. At the time of diagnosis they tended to have an immediate or dual asthmatic reaction and were younger than the other subjects. The asthmatic subjects had dual or late reactions at diagnosis. It was concluded that respiratory symptoms, isocyanate sensitization, and airway hyperresponsiveness may persist for some time after exposure to **toluene** diisocyanate has ended.
[Mapp CE et al; Am Rev Respir Dis 137 (6): 1326-9 (1988)]**PEER REVIEWED**

Six workers with occupational asthma due to **toluene** diisocyanate were studied. For each worker a detailed clinical and occupational history was taken, and lung function measurement and skin intradermal tests for common allergens were carried out. Methacholine inhalation challenge was performed before **toluene** diisocyanate inhalation, and 8 hr after **toluene** diisocyanate inhalation. Methacholine challenge was within normal limits when performed before **toluene** diisocyanate inhalation, but went into the asthmatic range after **toluene** diisocyanate inhalation. These cases provid evidence that asthma can be induced by **toluene** diisocyanate in the absence of airway hyperresponsiveness. They further demonstrate that an isolated negative methacholine inhalation test cannot be used to exclude sensitization to **toluene** diisocyanate. Screening and follow-up studies on workers exposed on **toluene** diisocyanate require serial measurements of airway responsiveness and of variable air-flow obstruction.
[Mapp CE et al; Eur J Respir Dis 68 (2): 89-95 (1986)]**PEER REVIEWED**

The clinical findings and the results of inhalation challenge with **toluene** diisocyanate and methacholine in 113 subjects with a history of exposure to **toluene** diisocyanate and work-related respiratory symptoms are reported. Only some of the subjects (40.7%) had isocyanate asthma, diagnosed by a positive **toluene** diisocyanate inhalation challenge. Most reactors had a dual (30.4%) or a late (41.3%) response. The interval between the last occupational exposure and the specific challenge was significantly shorter in reactors, and among this group the number of immediate reactions to **toluene** diisocyanate decr progressively with an incr interval. The reactors had a significantly higher proportion of positive responses to methacholine and a significantly lower mean PD[1][5] FEV[1] (provocative dose of methacholine which provoked a 15% decrease in forced expiratory volume in 1 second): reactors 557:g, SEM 92.3; non-reactors 1346:g, SEM 128, P < .01. Methacholine challenge could not identify

subjects with isocyanate asthma.
[Moscato G et al; J Occup Med 33 (6): 720-5 (1991)]**PEER REVIEWED**

Toluene diisocyanate is commonly used as the 2,4 and 2,6 isomers. NIOSH has estimated that 50,000 to 100,000 workers in the United States are regularly exposed to diisocyanates. As of 1977, 49,996 were estimated to be exposed to **toluene** diisocyanate alone. Methods for measuring diisocyanate exposures were considered. The current American Conference of Governmental Industrial Hygienists' recommended standard is 0.005 ppm time weighted average and 0.02 ppm peak for four 15 min periods a day. Results of exposure measurements taken in industry were summarized. Health effects of diisocyanates were discussed. In laboratory animals, **toluene** diisocyanate has caused inflammation and necrosis when applied directly to the skin, conjunctivitis when applied to the eyes, and rhinitis, laryngitis, tracheitis, bronchitis, and pneumonia when inhaled. Diisocyanates are potent pulmonary sensitizers capable of causing isocyanate asthma in humans. They can induce nonspecific airways disease and hypersensitivity pneumonitis after either acute or chronic exposure.
[Musk AW et al; Am J Ind Med 13 (3): 331-49 (1988)]**PEER REVIEWED**

A 46 yr old man who had worked in a paint processing plast for over 29 yr was admitted to our hospital with complaints of nocturnal dyspnea and dry cough. A chest X-ray film showed diffuse granular shadows in bilateral lungs. Pulmonary function tests revealed reduction of diffusing capacity and restrictive impairments. Hypersensitivity pneumonitis due to isocyanates was speculated from his occupational history and clinical course. Positive skin tests against **toluene** diisocyanate-human serum albumin and diphenylmethane diisocyanate-human serum albumin, precipitating antibody against **toluene** diisocyanate-human serum albumin, and negative lymphocyte stimulating tests of peripheral blood and bronchoalveolar lavage fluid were also noticed. Environmental provocation test was positive. Histological findings of transbronchial lung biopsy specimens showed diffuse alveolitis and Masson body, but no granulomas. According to these results, the patient was diagnosed as hypersensitivity pneumonitis due to **toluene** diisocyanate. Type III allergy of Gell-Coombs seems to participate in this case. The granulomatous lesion is seen less frequently in isocyanate related hypersensitivity pneumonitis than in hypersensitivity pneumonitis induced by organic dusts, which suggests the difference in immunological and histological reactions between both types of hypersensitivity pneumonitis.
[Nozawa S et al; Nippon Kyobu Shikkan Gakkai Zasshi 27 (11): 1335-41 (1989)]**PEER REVIEWED**

Pulmonary function tests were done and compared to current and past potential exposure levels of **toluene** diisocyanate for 57 **toluene** diisocyanate manufacturing workers and 89 workers not exposed to **toluene** diisocyanate or other known respiratory hazards. The average **toluene** diisocyanate plant experience was 4.1 yr (standard deviation = 2.8). Routine industrial hygiene measurements have shown **toluene** diisocyanate exposure below a time-weighted average of 0.005 ppm and a short-term exposure level of 0.02 ppm. A certified industrial hygienist ranked department and job classification by level of potential exposure to **toluene** diisocyanate (none, low, moderate, and high). A questionnaire was administered to determine the prevalence of respiratory symptoms and smoking habits. Using backward regression analysis, cumulative pack-years of cigarette smoking and prevalence of lower respiratory symptoms were statistically significant predictors of a standardized forced expiratory volume at 1 second; however, **toluene** diisocyanate exposure, whether classified as current, highest career level, cumulative, or cumulative highest-to-date, was not associated with a decline in forced expiratory volume.
[Olsen GW et al; J Occup Med 31 (8): 664-7 (1989)]**PEER REVIEWED**

Fifty seven polyurethane foam manufacturing workers and 24 reference workers were followed for 4 yr to clarify the effects on pulmonary function of working in polyurethane foam factories with exposure to **toluene** diisocyanate. No significant differences in the average annual losses of pulmonary function for 4 yr were observed among the 28 polyurethane foam workers whose **toluene** diisocyanate exposure levels were very low (mean = 0.1 ppb, group L), the remaining 29 polyurethane foam workers with mean **toluene** diisocyanate exposure of 5.7 ppb (group H), and the reference workers. However, 15 polyurethane foam workers in group H who had experienced peak exposure excursions to 30 ppb or above with a mean concn of 8.2 ppb showed significantly larger average annual losses in percentage maximal mid-expiratory flow, forced expiratory volume in 1 sec ratio to vital capacity, and forced expiratory flow at 25% of forced vital capacity than expected, and significantly larger average annual losses in some obstructive pulmonary function indices than those of the 14 remaining polyurethane foam workers in group H whose peak exposure excursion levels were 3-14 ppb with a mean time-weighted average of 1.7 ppb, group L, and the reference workers. These findings suggest that the peak exposure excursion level of **toluene** diisocyanate might be important in inducing obstructive pulmonary function changes in the polyurethane foam workers rather than the TWA exposure levels, though further comparative studies of the AAL in those who are exposed to different peak exposure excursion levels but the same mean exposure levels are necessary. From the standpoint of prevention, the proposition that peak exposure excursion levels exceeding 20 ppb should be avoided is reasonable.
[Omae K et al; Int Arch Occup Environ Health 63 (8): 565-9 (1992)]**PEER REVIEWED**

To evaluate the morphologic basis of the different outcomes of **toluene** diisocyanate asthma after quitting occupational exposure, ten patients with **toluene** diisocyanate asthma were examined who showed, at diagnosis, a positive **toluene** diisocyanate challenge test and nonspecific bronchial hyperresponsiveness to methacholine. After diagnosis, all patients ceased work and a 4 to 40 mo follow-up was obtained with three to eight determinations of the cumulative dose producing a 15% fall in forced expiratory volume in 1 second to methacholine in each patient. Bronchoalveolar lavage and biopsy of bronchial muscosa were performed 3 to 39 mo after cessation of work, in the absence of acute exacerbations of the disease. Total cell count in bronchoalveolar lavage fluid was moderately increased in four of ten patients, eosinophils were increased in five of ten patients, and neutrophils were increased in eight of ten patients. Mucosal biopsy specimens of main or lobar bronchi were available in eight of ten patients; epithelial damage and thickening of basement membrane was observed in almost all patients, as well as a mild to moderate inflammatory reaction in the submucosa, mainly represented by lymphocytes, eosinophils, and neutrophils. No relationship was observed between the cellularity of bronchoalveolar lavage and the degree of nonspecific bronchial hyperresponsiveness at the time of bronchoalveolar lavage; mean values of total cells and differential count were not different between patients with presence or absence of the different histologic findings. Mucosal biopsy and bronchoalveolar lavage were performed also in four subjects exposed to dusts without respiratory symptoms or nonspecific bronchial hyperresponsiveness; similar findings were obtained except for the absence of eosinophils in bronchoalveolar lavage and a lesser degree of basement membrane thickening and inflammatory reaction in the submucosa. The study of the changes in nonspecific bronchial hyperresponsiveness after quitting exposure showed that five of ten patients had a significant improvement in nonspecific bronchial hyperresponsiveness to methacholine, as evaluated by a positive significant linear regression between months of work cessation and forced expiratory volume in 1 sec of methacholine; only one of these five patients had an increased number of eosinophils in bronchoalveolar lavage fluid. By contrast, four of the five patients with persistent nonspecific bronchial hyperresponsiveness after quitting exposure had an

increased number of eosinophil in bronchoalveolar lavage. It is suggested that persistent nonspecific bronchial hyperresponsiveness in **toluene** diisocyanate asthma after cessation of work may be related to an inflammatory reaction in which eosinophil infiltration seems to be a major determinant.
[Paggiaro P et al; Chest 98 (3): 536-42 (1990)]**PEER REVIEWED**

The effect of cessation of exposure to **toluene** diisocyanate was studied in six patients with **toluene** diisocyanate induced asthma, proved by a positive inhalation challenge with **toluene** diisocyanate. Bronchial challenges with **toluene** diisocyanate and methacholine were performed, and lobar bronchial biopsies were taken at diagnosis and 6 mo later, after cessation of exposure. Biopsies from four nonasthmatic control subjects were also examined. At diagnosis, asthmatic subjects had thickened reticular basement membrane ($p < 0.05$) and increased numbers of mononuclear cells ($p < 0.05$) and eosinophils ($p < 0.05$) in the lamina propria when compared with control subjects. Electron microscopy showed degranulation of eosinophils and mast cells in asthmatics. Six months after cessation of exposure, the thickness of reticular basement membrane was significantly reduced compared with that at diagnosis ($p < 0.05$), and it decr to values similar to those of control biopsies. Inflammatory cell numbers in bronchial mucosa of asthmatic subjects did not change significantly 6 mo after removal from exposure, and degranulation of eosinophils and mast cells was still present. At the end of the study, airwa hyperresponsiveness to methacholine and/or sensitivity to **toluene** diisocyanate persisted in most of the asthmatic patients despite the cessation of exposure and the disappearance of asthmatic symptoms. In conclusion, in patients with occupational asthma induced by **toluene** diisocyanate, the avoidance of exposure to the sensitizing agent for 6 mo is able to reverse the reticular basement membrane thickening in the bronchial mucosa, but th inflammatory cell infiltrate, the specific sensitivity to **toluene** diisocyanate, and the nonspecific airway hyperreactivity may persist.
[Saetta M et al; Am Rev Respir Dis 145 (1): 169-74 (1992)]**PEER REVIEWED**

Forty-three workers exposed to low levels of **toluene** diisocyanate during the process of producing polyurethane forms were examined immunologically for immunoglobulin-G, A, M, and E and serum enzyme activities such as serum angiotensin converting enzyme, serum lysozyme and glycylproline dipeptidyl aminopeptidase. Air concn of **toluene** diisocyanate was annually measured in various places of work during the past five years from 1979 to 1983. The results obtained in the present study were as follows. The air concn of **toluene** diisocyanate at all places of work was below the permissible concn level of 0.02 ppm throughout the study period. Subjective symptoms and abnormal findings on chest X-ray considered directly related to **toluene** diisocyanate exposure were no observed. No remarkable abnormal findings in blood cell counts and in serum biochemical studies could be seen in any of the workers. The serum immunoglobulin-G levels in workers directly exposed to **toluene** diisocyanate were significantly higher ($p < 0.05$) than those in workers indirectly exposed to **toluene** diisocyanate and in non-exposed workers. In the study of serum enzymatic activity, serum lysozyme activity in workers exposed directly to **toluene** diisocyanate was significantly higher ($p < 0.01$) than those in workers indirectly exposed to **toluene** diisocyanate and in non-exposed workers.
[Taniwaki H et al; Sangyo Igaku 29 (2): 130-5 (1987)]**PEER REVIEWED**

A case of building related health complaints was investigated with respect to the relationship among frequency of symptoms, antibodies to albumin conjugates of formaldehyde, **toluene** diisocyanate, and trimellitic anhydride, and volatile organic chemicals. The indoor air concn of volatile organic chemicals, formaldehyde, **toluene** diisocyanate and trimellitic anhydride did not exceed Fed-OSHA and ACGIH permissible standards. However, formaldehyde concn ranged between 0.05 and 0.08 ppm. The reported

symptoms were multiple, involving the eyes, nose, sinuses, throat, lungs, skeletomuscular system and central nervous system. Anti-formaldehyde, **toluene** diisocyanate, and trimellitic anhydride isotypes were found in 12 of 14 full-time employees and were nondetectable in one part-time employee. The data suggest that a synergistic immunological response to airborne chemicals may be occurring in these subjects. In conclusion, immunological monitoring of affected individuals where chemicals are suspected may prove to be useful in future investigations of building related illness.
[Thrasher JD et al; Am J Ind Med 15 (2): 187-95 (1989)]**PEER REVIEWED**

Diisocyanate inhalation tests (maximal concn, 20 ppb; exposure time, 1-2 hr) were performed using **toluene** diisocyanate (TDI, n = 15) and diphenylmethane diisocyanate (MDI, n = 7) as well as methacholine challenges in 19 workers who had a clinical history of **toluene** diisocyanate/diphenylmethane diisocyanate induced asthma. Additionally volunteers were tested who had n previous contact with diisocyanates: 10 healthy individuals with a negative methacholine test and 14 patients with asthma and a positive methacholine test were exposed to **toluene** diisocyanate. In all, 1 of the normal volunteers and 3 of the patients with asthma unrelated to diisocyanates showed a positive airway reaction to **toluene** diisocyanate, and 13 of the 19 diisocyanate workers displayed a positive result in the **toluene** diisocyanate/diphenylmethane diisocyanate inhalation test; however, only 6 of these 13 individuals reacted to methacholine. Furthermore, 3 of the 6 patients with a negative **toluene** diisocyanate/diphenylmethane diisocyanate challenge test demonstrated a significant response to methacholine. It was concluded that bronchial hyperreactivity as evaluated by the methacholine challenge test is not closely related to isocyanate induced bronchoconstriction and, therefore, the metacholine challenge is only of limited diagnostic value in patients with suspected isocyanate induced asthma.
[Vogelmeier C et al; Int Arch Occup Environ Health 63 (1): 9-13 (1991)]**PEER REVIEWED**

An outbreak of occupational asthma due to **toluene** diisocyanate among industrial workers was described. Four employees at a velcro/like tape manufacturing factory in Taipei, Taiwan were seen in an outpatient clinic complaining of cough, shortness of breath, and wheezing. The symptoms became worse at night and improved after long holidays. The patients' job involved applying an adhesive to the tape. Thirty eight of 45 employees were interviewed by questionnaire and given pulmonary function tests. The pulmonary function tests were given during a workday, after a 10 day holiday, and 5 mo after control measures such as process isolation, improved ventilation, and substitution for **toluene** diisocyanate were instituted. Industrial hygiene sampling for **toluene** diisocyanate was conducted. Fourteen workers had symptoms of asthma or asthmatic bronchitis. The highest attack rate occurred in workers employed in the tape processing area where the adhesive was applied. Workers in the tape processing area also showed the greatest decr in 1 second forced expiratory volume and forced vital capacity over the workday. Mean **toluene** diisocyanate concn ranged from 0.012 to 0.047 ppm, the highest occurring in the tape processing area and the lowest in the weaving area. The prevalence of asthmatic symptoms was significantly correlated with **toluene** diisocyanate concn. The forced expiratory volume in 1 second and forced vital capacity values were significantly improved after the 10 day holiday and 5 mo after the control methods were instituted. No asthmatic symptoms were reported after 5 mo. It was concluded that **toluene** diisocyanate was responsible for the outbreak and improving the work environment was effective in reducing exposure to **toluene** diisocyanate.
[Wang JD et al; Am J Ind Med 14 (1): 73-8 (1988)]**PEER REVIEWED**

A 41 yr old automobile paint sprayer showed the clinical features of hypersensitivity pneumonitis 1 wk after he had begun to work with paint materials containing **toluene** diisocyanate. His symptoms began 6 to 8 hr after exposure to the agent and spontaneously disappeared by the next morning. He had diffuse, fine reticulonodular shadows on a chest roentgenogram and a restrictive impairment of pulmonary function. Immunoglobulin G antibody to **toluene** diisocyanate-human serum albumin was present in bronchoalveolar lavage fluid and sera: IgA antibody was present only in bronchoalveolar lavage fluid. Also, the patient had sensitized bronchoalveolar lymphocytes to **toluene** diisocyanate-human serum albumin. The histologic findings suggested hypersensitivity pneumonitis. The results of bronchoalveolar lavage, which was repeated on four separate occasions, showed lymphocytosis and a predominance of suppressor cytotoxic T cells. The findings from serial determinations of humoral antibodies showed no changes consistent with the results of clinical and laboratory studies. In contrast, blastogenic responses of bronchoalveolar lymphocytes to **toluene** diisocyanate markedly decr, and the patient showed clinical improvement despite continued exposure to the agent.
[Yoshizawa Y et al; Ann Intern Med 110 (1): 31-4 (1989)]**PEER REVIEWED**

TOLUENE DIISOCYANATE

CASRN: 26471-62-5

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Medical Surveillance:

A SCREENING PROGRAM WAS UNDERTAKEN AT A RESEARCH & DEVELOPMENT FACILITY OF A LARGE **TOLUENE**-DIISOCYANATE (TDI) MANUFACTURING CORPORATION. THE PURPOSE WAS TO DETERMINE THE OCCURRENCE OF ANTIBODIES TO TDI IN SELECTED WORKER POPULATIONS. NO TOLYL-REACTIVE IMMUNOGLOBULIN-E ANTIBODIES WERE DETECTED IN SERA WHEN WORKERS WERE EXPOSED ONLY TO AMBIENT TDI CONCN. WORKERS HAD ACUTE EXPOSURES TO TDI AS A RESULT OF SPILLS OR SPLASHES. ANTIBODY RESPONSES DEVELOPED IN 3 OF 4 INDIVIDUALS WHOSE ACUTE EXPOSURES WERE ACCOMPANIED BY IMMEDIATE RESPIRATORY SYMPTOMATOLOGY & A DECREASED FORCED EXPIRATORY VOLUME. AN ANTIBODY RESPONSE DEVELOPED IN 1 OF 9 WORKERS & IMMEDIATE RESPIRATORY SYMPTOMS, BUT NO SPIROMETRIC CHANGES UPON ACUTE TDI EXPOSURE. ROUTINE SEROLOGIC SCREENING OF WORKERS FOR TOLYL-REACTIVE ANTIBODIES MAY BE OF VALUE IN CONFIRMING SUSPECTED ISOCYANATE EXPOSURE & IN PROVIDING AN EARLY WARNING OF DEVELOPING TDI HYPERSENSITIVITY.
[KAROL MH; J OCCUP MED 23 (11): 741 (1981)]**PEER REVIEWED**

MEDICAL EVALUATIONS OF 15 WORKERS WERE MADE TO DETERMINE THE HEALTH EFFECTS OF EXPOSURE TO TDI, PHOSGENE & TDA. THE FOLLOWING STEPS WERE RECOMMENDED: THE ENTIRE FACTORY POPULATION SHOULD BE SURVEYED PERIODICALLY FOR SYMPTOMS OF LOWER RESPIRATORY TRACT DISEASES & LUNG FUNCTION ABNORMALITIES THAT MAY BE CAUSED BY CHEMICAL EXPOSURE; TDI EXPOSURE SHOULD BE ENDED FOR SENSITIZED WORKERS OR FOR THOSE WITH EXCESSIVE DECLINE IN LUNG FUNCTION.
[COSTELLO RJ, PETERS JM; HEALTH HAZARD EVALUATION DETERMINATION REPORT NO HE-78-31-623, OLIN CORPORATION, ASHTABULA, OHIO 44004; REPORT NIOSH-HE-78-31-623, ORDER NO PB80-195274 (1979)]**PEER REVIEWED**

/Protect/ from exposure those individuals with diseases of blood and liver. Physical exam of exposed personnel annually, incl blood count and liver functions. /**Toluene**-2,4-diisocyanate/
[ITII. Toxic and Hazardous Industrial Chemicals Safety Manual. Tokyo, Japan: The International Technical Information Institute, 1988. 528]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": Whenever medical surveillance is indicated, in particular when exposure to a carcinogen has occurred, ad hoc decisions should be taken concerning ... /cytogenetic and/or other/ tests that might become useful or mandatory. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 23]**PEER REVIEWED**

Comprehensive preplacement medical examinations should be given to each employee. The examination should include a pulmonary function test including FEV1, FVC, and FEV1/FVC, a history of diisocyanate exposure, smoking history, and history of respiratory conditions. The medical data obtained in the pre-placement examination can be used as a base line for periodic examination. Periodic examinations may be useful in detecting a reduction in lung function. Lung function tests, pulmonary history, and pulmonary physical exam should be repeated at least annually. All medical records, including pulmonary function and related medical tests, should be maintained for 30 years.
[Zenz, C. Occupational Medicine-Principles and Practical Applications. 2nd ed. St. Louis, MO: Mosby-Yearbook, Inc, 1988. 1019]**PEER REVIEWED**

TOLUENE DIISOCYANATE

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Probable Routes of Human Exposure:

Exposure to **toluene** diisocyanate is primarily occupational via inhalation or dermal contact with the aerosol or vapor. Workers may also be exposed through skin contact with freshly cured foam or as a result of spills or splashes. (SRC)
PEER REVIEWED

THE RESPIRATORY HEALTH OF 277 WORKERS IN A NEW **TOLUENE** DIISOCYANATE (TDI) MANUFACTURING PLANT WAS STUDIED PROSPECTIVELY DURING 5 YR OF EXPOSURE. PERSONAL TDI MONITORS WERE USED TO CONTINUOUSLY MEASURE PEAK & 8-HR TIME-WEIGHTED AVG (TWA) CONCN IN MORE THAN 2000 SAMPLES. REGRESSION OF ANNUAL CHANGE ON SMOKING (PACK-YEARS), ATOPIC STATUS & CUMULATIVE TDI EXPOSURE, DICHOTOMIZED AT 68.2 PPB MONTHS INTO LOW & HIGH EXPOSURE GROUPS, SHOWED SIGNIFICANT EFFECTS OF SMOKING ON SPIROMETRIC TESTS & LUNG VOLUMES. AFTER ADJUSTING FOR PACK-YEARS OF SMOKING, THE 74 MEN IN THE HIGH CUMULATIVE TDI EXPOSURE CATEGORY HAD SIGNIFICANTLY LARGER DECLINE IN FEV1 (1-S FORCED EXPIRATORY VOLUME), % FEV (% FORCED EXPIRATORY VOLUME) & FEF25-75% (FORCED EXPIRATORY FRACTION FROM 25 TO 75% VITAL CAPACITY) THAN DID THE 149 MEN IN THE LOW CATEGORY. ANNUAL CHANGE IN FEV1 WAS THEN EXAMINED IN 6 SMOKING-EXPOSURE CATEGORIES: IN NEVER-SMOKERS, AVG ANNUAL DECLINE WAS 38 ML/YR GREATER IN THOSE WITH HIGHER CUMULATIVE TDI EXPOSURE.
[DIEM JE ET AL; AM REV RESPIR DIS 126 (3): 420 (1982)]**PEER REVIEWED**

VAPORS OF THESE COMPD INVARIABLY BECOME AIRBORNE IN POLYMERIZATION REACTIONS, ESP SINCE HEAT & GAS ARE EVOLVED. /**TOLUENE** DIISOCYANATES/
[Hamilton, A., and H. L. Hardy. Industrial Toxicology. 3rd ed. Acton, Mass.: Publishing Sciences Group, Inc., 1974. 335]**PEER REVIEWED**

NIOSH (NOHS Survey 1972-1974) has statistically estimated that 29,284 workers are exposed to TDI in the USA(1). NIOSH (NOES Survey 1981-1983) has statistically estimated that 6,044 workers are exposed to TDI in the USA(2). Since the NOES survey excludes exposure to trade name chemicals which may contain the chemical, occupational exposure could be considerably higher(SRC).
[(1) NIOSH; National Occupational Health Survey (1974) (2) NIOSH; National Occupational Exposure Survey (1983)]**PEER REVIEWED**

Concentration medians for 2,4-**toluene** diisocyanate in 2 plants producing flexible polyurethane foam were 0.70 and 0.33 ppb for the mixing and finishing ends, respectively(1). The respective median values for 2,6-TDI were 0.91 and 1.1 ppb. Maximum concentrations of 2,6-TDI exceeded 64 ppb at the finishing end(1).
[(1) Rando RJ et al; Am Ind Hyg Assoc J 45: 199-203 (1984)]**PEER REVIEWED**

In a Finnish study, TDI vapor concentrations ranged from 25-80 ug/cu m for pouring, 14-44 ug/cu m for paper stripping, and 1-8 ug/cu m for cutting(1). Personal monitors measured 9-34 ug/cu m and 5-30 ug/cu m of the 2,4-isomer for pouring and paper stripping, respectively(1). While 2,4-**toluene** diisocyanate constitutes 80% of TDI, and 2,6-**toluene** diisocyanate 20%, the 2,4-isomer is more reactive so that the concentration of the 2,6-isomer is higher in workplace air(1). The percentage of 2,4-**toluene** diisocyanate to total **toluene** diisocyanate measured with the personal monitors ranged from 29 to 69%(1). TDI levels of 1.3-2.8 ppb were detected in air inside a Swedish factory manufacturing polyurethanes(2).
[(1) Rosenberg C, Savolainen H; J Chromatography 367: 385-92 (1986) (2) Audunsson G et al; Intern J Environ Anal Chem 20: 85-100 (1985)]**PEER REVIEWED**

Mean concn ranges of TDI reported in ambient workplace air were 0.7-710 ug/cu m in TDI production, ND - 1490 ug/cu m during polyurethane foam production, 70-140 mg/cu m during elastomer production, 13 - 1050 ug/cu m during polyurethane foam use, 10-710 ug/cu m during polyurethane spray paint use, and <1-740 ug/cu m during the production of polyurethane-coated wire(1). Mean concn in personal samples ranged from ND-540 ug/cu m during polyurethane foam production and 2-1220 ug/cu m during polyurethane spray foam use(1). Additionally, mean concn of TDI released from insulation in a ship's hold was reported to be 120-150 ug/cu m and that released from coated fabric in a workplace 2-10 ug/cu m(1). During the outdoor application of TDI foam to a 40 ft diameter storage tanks, the mean atmospheric TDI concentration downwind from the spray gun was 0.3 ppm at 8 ft, 0.02 ppm at 40 ft, and 0.002 ppm at 150 ft(2). TDI was not detected more than 8 ft upwind of the spray gun(2). Air samples taken within two ft of the foam surface immediately after spraying had ceased was found to be 0.03 ppm(2). Mean TDI concentrations near the pumping equipment during material transfer was 0.02 ppm(2).
[(1) IARC Monograph on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. 39: 287-323 (1985) (2) Peterson JE et al; Amer Id Hyg Assoc J 23: 345-52 (1962)]**PEER REVIEWED**

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Emergency Medical Treatment:

Emergency Medical Treatment:

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The following Overview, *** **TOLUENE** DIISOCYANATE ***, is relevant for this HSDB record chemical.

Life Support:

- This overview assumes that basic life support measures have been instituted.

Clinical Effects:

SUMMARY OF EXPOSURE

0.2.1.1 ACUTE EXPOSURE

- **Toluene** diisocyanate is an irritant to skin, lungs, conjunctiva and gastrointestinal tract. Euphoria, ataxia, mental aberrations, sensitization (primarily respiratory), bronchitis, emphysema and cor pulmonale can occur.

HEENT

0.2.4.1 ACUTE EXPOSURE

- Severe conjunctival irritation and lacrimation from liquid or high vapor concentrations is likely. Lower concentrations may produce a burning or prickling sensation.
- Glaucoma and iridocyclitis have been reported with a splash accident.

RESPIRATORY

0.2.6.1 ACUTE EXPOSURE

- Burning or irritation of the nose and throat, cough, laryngitis, chest pain, and asthmatic syndrome (chemical bronchitis with severe bronchospasm), sensation of oppression or constriction of the chest, bronchitis, emphysema and cor pulmonale may occur.

- Respiratory symptoms may recur several years after discontinuation of exposure.

NEUROLOGIC

0.2.7.1 ACUTE EXPOSURE

- Acute exposures may produce headache, insomnia, euphoria, ataxia, anxiety neurosis with depression, or paranoid tendencies.

GASTROINTESTINAL

0.2.8.1 ACUTE EXPOSURE

- Inhalation of vapor or aerosol may produce vomiting and abdominal pain. Epigastric and substernal pain may be secondary to the paroxysmal or persistent cough associated with inhalation.

DERMATOLOGIC

0.2.14.1 ACUTE EXPOSURE

- Irritation and inflammation are common. Dermal absorption is low.

IMMUNOLOGIC

0.2.19.1 ACUTE EXPOSURE

- Elevated specific IgE and IgG antibodies have been detected in sensitized and exposed workers. The presence of antibodies does is an indicator of exposure but not of sensitization.

CARCINOGENICITY

0.2.21.1 IARC CATEGORY

- **Toluene** diisocynate has been classified as a 2B agent: possibly carcinogenic to humans, based on sufficient evidence of carcinogenicity in experimental animals and no human data (IARC, 1987).

0.2.21.2 HUMAN OVERVIEW

- **Toluene** diisocyanate is considered a suspected or possible human carcinogen, based on sufficient evidence of carcinogenicity or tumors (spleen, subcutaneous, hepatic, ovarian, peritoneum, mammary gland tissues) in experimental animals (IARC, 1987; US DHHS, 1994; ACGIH, 1995).

Laboratory:

- Monitor respiratory function closely.

Treatment Overview:

ORAL EXPOSURE

- Due to the irritant nature of this substance, emesis is not advised.
- DILUTION: Immediately dilute with 4 to 8 ounces (120 to 240 mL) of milk or water (not to exceed 15 mL/kg in a child).
- ACTIVATED CHARCOAL: Administer charcoal as slurry (240 mL water/30 g charcoal). Usual dose: 25 to 100 g in adults/adolescents, 25 to 50 g in children (1 to 12 years), and 1 g/kg in infants less than 1 year old.
- Monitor patient for respiratory distress. If a cough or difficulty in breathing develops, evaluate for respiratory tract irritation, bronchitis and pneumonia.
- Allergic reaction: Sensitized individuals should be cautioned to avoid further exposure as serious allergic reactions may result.

INHALATION EXPOSURE

- DECONTAMINATION: Move patient to fresh air. Monitor for respiratory distress. If cough or difficulty in breathing develops, evaluate for respiratory tract irritation, bronchitis, or pneumonitis. Administer 100 percent humidified supplemental oxygen with assisted ventilation as required.
- Randomized, double-blind cross-over studies showed minimal efficacy of bronchodilators. This could be due to the absence of airway hyperresponsiveness in some TDI-induced asthma.

EYE EXPOSURE

- DECONTAMINATION: Exposed eyes should be irrigated with copious amounts of tepid water for at least 15 minutes. If irritation, pain, swelling, lacrimation, or photophobia persist, the patient should be seen in a health care facility.

DERMAL EXPOSURE

- DECONTAMINATION: Wash exposed area extremely thoroughly with soap and water. A physician may need to examine the area if irritation or pain persists.

Range of Toxicity:

- Available dose-response information concerning humans pertains to inhalational exposure. Concentrations of 2.5 ppm are considered Immediately Dangerous to Life or Health. A fatality in an asthmatic who continued exposure to TDI has been reported.
- The recommended short term exposure limits for TDI in industry is 0.02 ppm. TDI does not have sufficient warning properties (e.g. odor or eye irritancy) at air concentrations below the recommended short term exposure limit.

[Rumack BH: POISINDEX(R) Information System. Micromedex, Inc., Englewood, CO, 2001; CCIS Volume 107, edition exp February, 2001. Hall AH & Rumack BH (Eds):TOMES(R) Information System. Micromedex, Inc., Englewood, CO, 2001; CCIS Volume 107, edition exp February, 2001.] **PEER REVIEWED**

Antidote and Emergency Treatment:

Noncardiogenic pulmonary edema and bronchospasm are the most immediate serious clinical consequences of isocyanate exposure. Markedly symptomatic patients should receive oxygen, ventilatory support, and an intravenous line. Treatment for asthma includes inhaled sympathomimetics (salbutamol, metaproterenol), intravenous theophylline, parenteral sympathomimetics (epinephrine, terbutaline), and steroids. /Isocyanates/
[Ellenhorn, M.J. and D.G. Barceloux. Medical Toxicology - Diagnosis and Treatment of Human Poisoning. New York, NY: Elsevier Science Publishing Co., Inc. 1988. 881]**PEER REVIEWED**

Copiously irrigate contaminated skin and eyes with saline. Few medical data are available to guide gut decontamination. Activated charcoal (1 g/kg) and a cathartic (sorbitol, magnesium citrate) may be useful for ingestions. /Isocyanates/
[Ellenhorn, M.J. and D.G. Barceloux. Medical Toxicology - Diagnosis and Treatment of Human Poisoning. New York, NY: Elsevier Science Publishing Co., Inc. 1988. 881]**PEER REVIEWED**

Most treatment is symptomatic. Mydriatics, systemic analgesics, and topical antibiotics (Sulamyd) may be used for corneal abrasions. There is no effective therapy for sensitized workers, and these people should be moved to a work site devoid of exposure to isocyanates. /Isocyanates/
[Ellenhorn, M.J. and D.G. Barceloux. Medical Toxicology - Diagnosis and Treatment of Human Poisoning. New York, NY: Elsevier Science Publishing Co., Inc. 1988. 881]**PEER REVIEWED**

Any employee who begins to experience shortness of breath during a shift should be removed from work immediately and should not return to work until pulmonary function tests have returned to base line. As is the case with asthma of any type, pulmonary function recovery may lag behind symptom recovery and take up to eight weeks to return to normal. If sensitized, the individual should not return to work in a TDI

area or work with any other isocyanate.
[Zenz, C. Occupational Medicine-Principles and Practical Applications. 2nd ed. St. Louis, MO: Mosby-Yearbook, Inc, 1988. 1020]**PEER REVIEWED**

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Animal Toxicity Studies:

Evidence for Carcinogenicity:

No data are available in humans. Sufficient evidence of carcinogenicity in animals. OVERALL EVALUATION: Group 2B: The agent is possibly carcinogenic to humans.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. S7 72 (1987)]**PEER REVIEWED**

Non-Human Toxicity Excerpts:

THE POSSIBILITY OF DERMAL EXPOSURES TO **TOLUENE** DIISOCYANATE RESULTING IN PULMONARY SENSITIVITY WAS INVESTIGATED USING GUINEA PIGS AS AN ANIMAL MODEL. **TOLUENE** DIISOCYANATE (1-100% CONCN) WAS APPLIED TO DORSAL SITES ON GUINEA PIGS, WHERE SKIN SENSITIVITY TO TDI WAS APPARENT BY THE 7TH DAY. AFTER 14 DAYS, ANIMALS WERE ADDNL EVALUATED FOR TDI SENSITIVITY BY SEROLOGIC ANALYSIS & BRONCHIAL PROVOCATION CHALLENGE. ANTIBODIES TO **TOLUENE** DIISOCYANATE WERE DETECTED USING PASSIVE CUTANEOUS ANAPHYLAXIS, DOUBLE DIFFUSION IN GEL, & RADIOLABELED ANTIGEN BINDING ASSAYS. ANTIBODIES WERE SPECIFIC FOR **TOLUENE** DIISOCYANATE. THE DEVELOPMENT OF RESPIRATORY HYPERSENSITIVITY AS A RESULT OF DERMAL CONTACT WITH **TOLUENE** DIISOCYANATE EMPHASIZES THE IMPORTANCE OF CAREFUL WORKPLACE PRACTICES & SUGGESTS REEVALUATION OF THE ROLE OF INHALATION &/OR DERMAL CONTACT IN CAUSING PULMONARY SENSITIZATION OF WORKERS.
[KAROL MH ET AL; TOXICOL APPL PHARMACOL 58 (2): 221 (1981)]**PEER REVIEWED**

TOLUENE DIISOCYANATE WAS MUTAGENIC IN SALMONELLA TYPHIMURIUM STRAINS TA1538 & TA98 AFTER METABOLIC ACTIVATION.
[ANDERSEN M ET AL; SCAND J WORK ENVIRON HEALTH 6 (3): 221 (1980)]**PEER REVIEWED**

GROUPS OF MALE & FEMALE RATS & MICE WERE EXPOSED TO 0.05 & 0.15 PPM OF 2,4/2,6-**TOLUENE**-DIISOCYANATE (80/20) BY INHALATION FOR 6 HR/DAY, 5 DAYS/WEEK FOR 2 YR. TYPE & INCIDENCE OF TUMORS & THE NUMBER OF TUMOR-BEARING ANIMALS OF EITHER SPECIES DID NOT INDICATE ANY CARCINOGENIC EFFECT. HEMATOLOGY, BIOCHEMISTRY, URINALYSIS, & CYTOGENICITY STUDIES DID NOT REVEAL ANY UNTOWARD EFFECT. INCREASED MORTALITY (FEMALES ONLY), REDUCED WEIGHT GAIN & SIGNS OF IRRITATION IN THE UPPER & LOWER RESPIRATORY TRACT RESULTED FROM EXPOSURE TO **TOLUENE** DIISOCYANATE IN THE MOUSE STUDY WITH THE HIGHEST INCIDENCE IN THE 0.15 PPM EXPOSURE LEVEL.

[LOESER E; TOXICOL LETT (AMST) 71 (1983)]**PEER REVIEWED**

EXPOSURE BY INHALATION TO 70 MG/CU M (10 PPM) ... 2,6-TDI OR 65/35 MIXT FOR 6 HR/DAY FOR 3-5 DAYS WAS LETHAL TO RATS; EXPOSURE TO 35 MG/CU M (5 PPM) OF MIXT FOR 4 DAYS KILLED 65% OF RATS.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V19 310 (1979)]**PEER REVIEWED**

LC50 FOLLOWING EXPOSURE ... FOR 14 DAYS WAS: MOUSE, 70 MG/CU M ... GUINEA PIG, 90 MG/CU M ... & RAT, 100 MG/CU M ... LC50 FOLLOWING EXPOSURE FOR 7 DAYS WAS 80 MG/CU M ... IN RABBITS. ... MICE, RATS & GUINEA PIGS EXHIBITED LACRIMATION, SALIVATION, RESTLESSNESS & HYPERACTIVITY.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V19 310 (1979)]**PEER REVIEWED**

ACUTE 6-HR INHALATION STUDIES IN RATS, CONCN OF 4200 MG/CU M ... WAS LETHAL, WHEREAS 420 MG/CU M ... WAS NOT. ANIMALS THAT DIED SHOWED ACUTE PULMONARY CONGESTION & EDEMA.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V19 310 (1979)]**PEER REVIEWED**

FOLLOWING EXPOSURE BY INHALATION ... TO 0.7 MG/CU M (0.1 PPM) ... FOR 6-HR ... 1 DAY/WK FOR 38 WK, OR ... 6 HR/DAY ON 5 DAYS/WK FOR ... 58 EXPOSURES, RAT SHOWED PROLIFERATION OF FIBROUS TISSUE ... OF BRONCHIOLES AS WELL AS PNEUMONITIS, TRACHEITIS & BRONCHITIS. IN RABBITS & GUINEA PIGS, NO PROLIFERATION ... .
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V19 310 (1979)]**PEER REVIEWED**

ACUTE SKIN ABSORPTION TESTS ... ON RABBITS PRODUCED SEVERE LOCAL IRRITATION BUT FAILED TO KILL, EVEN WITH DOSES AS HIGH AS 16 G/KG BODY WT ... NO ANATOMICAL INJURY TO INTESTINAL ORGANS.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V19 310 (1979)]**PEER REVIEWED**

TEST APPLICATION OF DROP OF META & PARA TOLUENEDIISOCYANATES ON RABBIT EYES CAUSED IMMEDIATE PAIN, LACRIMATION, SWELLING OF LIDS, & CONJUNCTIVAL REACTION. HOWEVER, CORNEAL EPITHELIUM WAS ONLY MILDLY DAMAGED ... /MIXT OF 2,4- & 2,6-ISOMERS/

[Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986. 929]**PEER REVIEWED**

EXPOSURE OF GUINEA PIGS BY INHALATION TO 14-35 MG/CU M (2-5 PPM) ... IN AIR ... 6 HR/DAY FOR 3 DAYS RENDERED THEM MORE SENSITIVE WHEN 3 WK LATER THEY WERE EXPOSED TO 0.14 MG/CU M (0.02 PPM) FOR 5 HR, AS SHOWN BY MORE PRONOUNCED REDN OF BREATH RATE ... COMPARED WITH ANIMALS ... NOT ... PREVIOUSLY EXPOSED.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V19 310 (1979)]**PEER REVIEWED**

Groups of 120 male and 120 female CD-1 mice, three to four weeks old, were exposed to 0, 0.05, or 0.15 ppm (0, 0.36 or 1.07 mg/cu m) production grade **toluene** diisocyanate (approx 80% 2,4 isomer & 20% 2,6 isomer) in an inhalation chamber for 6 hr/day on 5 days/wk for 104 wk. There was a significant reduction in body weight in the high-dose group /sex not stated/ and a significant increase in mortality in both high and low-dose females by the termination of the study. No such effect was seen in males. Neither the types of tumor observed nor their incidences were dose-related, and both corresponded to those seen in historical controls for this strain of mice. However, dose-related pathological changes were observed in the nasal cavity (chronic or necrotic rhinitis), together with changes in the lower respiratory tract (interstitial pneumonia, catarrhal bronchitis) in both groups.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 303 (1986)]**PEER REVIEWED**

Groups of 126 male and 126 female Sprague Dawley CD rats, six to nine weeks old, were exposed to 0, 0.05 or 0.15 ppm (0, 0.36 or 1.07 mg/cu m) production-grade **toluene** diisocyanate (approx 80% 2,4 isomer and 20% 2,6 isomer) in an inhalation chamber for 6 hr/day on 5 days/wk for 108 wk or 110 wk. A significant reduction in weight gain was observed during the first 12 wk of the study among the high-dose animals of each sex, but body wt gain was similar in all groups thereafter. No significant difference in mortality between treated and control groups of either sex was reported. Tumor incidences and types were reported to be similar in control and treated groups.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 304 (1986)]**PEER REVIEWED**

Rats receiving up to 240 mg/kg **toluene** diisocyanate by gavage daily on 5 days/wk for 13 wk were found to suffer from mild to moderate bronchopneumonia.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 306 (1986)]**PEER REVIEWED**

In dogs, a correlation has been made between immunological and respiratory responses to **toluene** diisocyanate. Dogs exposed once every second week for 41 wk to 1 mg/kg **toluene** diisocyanate

delivered as an aerosol intratracheally developed a systemic immune response to **toluene** diisocyanate conjugated with dog serum albumin as well as immediate-type airway responses.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 307 (1986)]**PEER REVIEWED**

The **toluene** diisocyanate induced delayed type hypersensitivity reaction in the ear of male mice was investigated and compared with the picryl chloride induced one. The results obtained were as follows: 1) When 1% **toluene** diisocyanate solution (20 ul/ear) as a challenging concentration was used for 7 week old ICR mice, distinct ear swelling was observed in every group sensitized with various concentrations (1-5%, 100 ul/animal) of **toluene** diisocyanate solution, and the swelling rate was the same or higher than that of picryl chloride induced delayed type hypersensitivity. 2) Five, 7 and 13 week old ICR mice showed a similar high response in TDI induced delayed type hypersensitivity, whereas the reactivity of 16 week old ICR mice was significantly lower than that of the above mentioned younger mice. 3) In both **toluene** diisocyanate and picryl chloride induced delayed type hypersensitivity reaction, ICR and BALB/c mice showed a similar high response, whereas the reactivity of ddY mice was significantly lower. The effects of dexamethasone and indomethacin were investigated with the **toluene** diisocyanate induced delayed type hypersensitivity model. The delayed type hypersensitivity reaction was suppressed significantly by both drugs, but the suppressive effects of dexamethasone were higher than that of indomethacin. All the above results indicate that the **toluene** diisocyanate induced delayed type hypersensitivity model in mice taking dye leakage as an index may be useful for evaluation of drugs for disorders derived from delayed type hypersensitivity reactions.
[Tominaga M et al; Jpn J Pharmacol 39 (2): 163-71 (1985)]**PEER REVIEWED**

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[Gordon T et al; Am Rev Respir Dis 132 (5): 1106-12 (1985)]**PEER REVIEWED**

The effect of exposure to **toluene** diisocyanate vapor on pulmonary performance was studied in guinea pigs. Female English smooth haired guinea pigs were exposed to 1.4 ppm **toluene** diisocyanate vapor or air for 3 hours per day for 4 days, or to 0.02 ppm **toluene** diisocyanate for 6 hours per day for 70 days. Pulmonary performance was evaluated by the ventilatory response of the animals to 10% carbon dioxide. Serum antibodies to **toluene** diisocyanate were measured on days 22 and 50 and **toluene** diisocyanate pulmonary hypersensitivity was measured on days 37 and 38. Lung tissue histopathology was evaluated in all animals on day 50 following **toluene** diisocyanate exposure. Pulmonary response to 10% carbon dioxide diminished by 30 to 50% following **toluene** diisocyanate exposures at 1.4 ppm up to day 14. The ventilatory response showed recovery during the next 5 weeks. In contrast, animals exposed to 0.02 ppm **toluene** diisocyanate daily for 70 days showed no change in ventilatory response, nor did control animals that were not exposed to **toluene** diisocyanate. Antibodies were detected on day 22 and pulmonary hyprsensitivity to **toluene** diisocyanate was found in all animals exposed to 1.4 ppm **toluene** diisocyanate. No antibodies to **toluene** diisocyanate nor pulmonary hypersensitivity were detected in animals exposed to 0.02 ppm **toluene** diisocyanate or in control animals. Lung tissue on day 50 in the 1.4 ppm **toluene** diisocyanate exposed animals showed multifocal subchronic interstitial inflammation, localized pleural thickening, and peripheral lymphoid hyperplasia. No apparent abnormalities were observed in lung tissue of the 0.02 ppm exposed group. Exposure to 1.4 or 0.02 ppm **toluene** diisocyanate resulted in measurable and no apparent pulmonary toxicity in guinea pigs, respectively. The 10 percent carbon dioxide challenge provide several advantages for measuring pulmonary function.
[Wang KL et al; J Toxicol Environ Health 15 (1): 137-48 (1985)]**PEER REVIEWED**

Groups of 50 F344/N rats of each sex and 50 B6C3F1 mice of each sex were gavaged with corn oil or a mixture of **toluene** diisocyanate in corn oil for 5 days per wk for 105 or 106 wk. Female rats and mice were given doses of 60 or 120 mg/kg body weight, while male rats received 30 or 60 mg/kg, and male

mice received 120 or 240 mg/kg. The **toluene** diisocyanate reacted with the moisture in the corn oil vehicle resulting in doses that were 10% to 23% below the target dose concn. The chemical product used was commercial grade **toluene** diisocyanate, which was an 80%-20% mixture of the 2,4- and 2,6-isomers. Chemical disposition and metabolism studies were conducted with each of the radiolabelled **toluene** diisocyanate isomers in male rats. Absorption of both of the **toluene** diisocyanate isomers occurred, with the highest concn found in the stomach, cecum, large intestine, and bladder. Excretion occurred via the feces and urine. The major metabolic products from the metabolism of 2,4-**toluene** diisocyanate were shown to be identical with those from the metabolism of the carcinogen, 2,4-diaminotoluene, whereas the metabolism of the 2,6-**toluene** diisocyanate isomer yielded one major product, identified as 2,6-bis(acetylamino)**toluene**. Greater than 10% depression in body weight gain occurred in all dosed groups of rats throughout most of the study. The major non-neoplastic lesions that were observed in both sexes of the **toluene** diisocyanate exposed rats were dose related incr in acute broncho-pneumonia, characterized as chemical pneumonitis, with incidences as high as 50%. In mice mean body weight gain was depressed in dosed male and in high dose females. The principle non-neoplastic lesion in mice that was attributed to chemical treatment was cytomegaly of the kidney tubular epithelium in males. Survival in all groups of dosed rats was significantly lower than in controls. A dose-dependent pattern of mortality did not commence until 70 wk of exposure, demonstrating that **toluene** diisocyanate elicited a cumulative toxic response. There was also significantly lower survival in high dose male, but not female mice, by comparison to controls. Despite the reduction of power and sensitivity in the rat studies caused by early mortality, statistically significant incr in tumor incidences were observed in many different target organs. **Toluene** diisocyanate was carcinogenic in F344/N rats, causing sc fibromas and fibrosarcomas in males and females, pancreatic acinar cell adenomas in males, and pancreatic islet cell adenomas, neoplastic nodules of the liver, and mammary gland tumors in females.
[Dieter MP et al; Toxicol Ind Health 6 (6): 599-621 (1990)]**PEER REVIEWED**

Toluene diisocyanate is a causative agent in occupational asthma. Through an oral catheter **toluene** diisocyanate, 0.03 ul, dissolved in 0.02 ml olive oil, was superfused on the tracheobronchial mucosa of anaesthetized guinea pigs. **Toluene** diisocyanate induced plasma exudation into both airway tissue and lumen (peak effect: 5 hr; duration approximately 17 hr). Light microscopy examinations demonstrated that the epithelium was not disrupted by this process (and that microvessels are abundant just beneath the epithelium). At days 6 and 21 after exposure to **toluene** diisocyanate PAS-positive cells were increased, but no other histological alterations were found. Also, the occurrence of peptide containing nerve fibres was not altered by **toluene** diisocyanate. After **toluene** diisocyanate exposure the airway smooth muscle tone was elevated as examined in vitro at base-line and at conc response to carbachol. The largest incr in tone were recorded 21 days after exposure to **toluene** diisocyanate. The abnormally large tone was not associated with an increased thickness of the smooth muscle layer nor was it associated with reduced effects of either beta 2-agonist (terbutaline) or xanthine (theophylline) relaxants. It is concluded that **toluene** diisocyanate induced plasma exudation into guinea pig airways for 17 hr without disrupting the epithelial lining and without causing major changes in the airway peptidergic innervation. Both the airway tone, and the number of mucous cells, are increased for at least 3 wk after exposure to **toluene** diisocyanate.
[Persson CG et al; Clin Exp Allergy 21 (6): 715-24 (1991)]**PEER REVIEWED**

Toluene diisocyanate was mutagenic in Salmonella typhimurium strains TA98 and TA100 in the presence (but not the absence) of Aroclor 1254-induced male Sprague Dawley rat or male Syrian hamster liver S9; it was not mutagenic in strains TA 1535 or 1537.
[DHHS/NTP; Toxicology and Carcinogenesis Studies of Commercial Grade 2,4 (80%) and 2,6 (20%) - Toluene Diisocyanate (Gavage Studies) p. 7 (1986) Technical Rpt Series No. 251 NIH Pub No. 86-2507]**PEER REVIEWED**

National Toxicology Program Studies:

Groups of 50 female F344/N rats and 50 female B6C3F1 mice were administered commercial grade **toluene** diisocyanate (80% 2,4- and 20% 2,6-) in corn oil by gavage at doses of 60 or 120 mg/kg body weight, 5 days per week for 105 or 106 weeks. Groups of 50 male F344/N rats received 30 or 60 mg/kg and groups of 50 male B6C3F1 mice received 120 or 240 mg/kg on the same schedule. Dosage analyses of **toluene** diisocyanate indicated that the chemical had reacted in the corn oil vehicle, resulting in actual gavage concentrations 77% to 90% of theoretical values. Groups of 50 rats and 50 mice of each sex received corn oil only and served as vehicle controls. Survival in all groups of dosed rats in the 2-year studies was shorter (P less than or equal to 0.005) than that of the controls; depressions in mean body weight gain relative to controls were greater than 10% in all dosed rat groups throughout most of the study. A dose-dependent pattern of cumulative toxicity began at 70 weeks and culminated in excessive mortality, indicating the estimated maximum tolerated dose had been exceeded for rats. Acute bronchopneumonia occurred at increased incidences in groups of dosed male and female rats (males: control, 2/50; low dose, 6/50; high dose, 14/50; females: 1/50, 10/50, 25/49). /Results indicated that/ commercial grade **toluene** diisocyanate in corn oil was carcinogenic for F344/N rats, causing subcutaneous fibromas and fibrosarcomas (combined) in males and females, pancreatic acinar cell adenomas in males, and pancreatic islet cell adenomas, neoplastic nodules of the liver, and mammary gland fibroadenomas in females. **Toluene** diisocyanate was not carcinogenic for male B6C3F1 mice. TDI was carcinogenic for female B6C3F1 mice, causing hemangiomas or hemangiosarcomas (combined), as well as hepatocellular adenomas.
[DHHS/NTP; Toxicology and Carcinogenesis Studies of Commercial Grade 2,4 (80%) and 2,6 (20%) - Toluene Diisocyanate (Gavage Studies) p. 7 (1986) Technical Rpt Series No. 251 NIH Pub No. 86-2507]**PEER REVIEWED**

Non-Human Toxicity Values:

LC50 Rat inhalation 56.96 mg/cu m/1 hr
[WHO; Environmental Health Criteria 75: Toluene Diisocyanates p. 33 (1987)]**PEER REVIEWED**

LC50 Rat inhalation 98.96 + or - 8.6 mg/cu m/4 hr
[WHO; Environmental Health Criteria 75: Toluene Diisocyanates p. 33 (1987)]**PEER REVIEWED**

LC50 Rat (male) inhalation 348.88 mg/cu m/4 hr
[WHO; Environmental Health Criteria 75: Toluene Diisocyanates p. 33 (1987)]**PEER REVIEWED**

LC50 Rat (female) inhalation 356 mg/cu m/4 hr
[WHO; Environmental Health Criteria 75: Toluene Diisocyanates p. 33 (1987)]**PEER REVIEWED**

LC50 Mouse inhalation 69.1 + or - 9.96 mg/cu m/4 hr
[WHO; Environmental Health Criteria 75: Toluene Diisocyanates p. 33 (1987)]**PEER REVIEWED**

LC50 Rabbit inhalation 78.32 mg/cu m/4 hr
[WHO; Environmental Health Criteria 75: Toluene Diisocyanates p. 33 (1987)]**PEER REVIEWED**

LC50 Guinea pig inhalation 90.4 + or - 19.2 mg/cu m/4 hr
[WHO; Environmental Health Criteria 75: Toluene Diisocyanates p. 33 (1987)]**PEER REVIEWED**

LD50 Rat oral 3060 mg/kg
[WHO; Environmental Health Criteria 75: Toluene Diisocyanates p. 33 (1987)]**PEER REVIEWED**

TOLUENE DIISOCYANATE

CASRN: 26471-62-5

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Non-Human Toxicity Excerpts:

THE POSSIBILITY OF DERMAL EXPOSURES TO **TOLUENE** DIISOCYANATE RESULTING IN PULMONARY SENSITIVITY WAS INVESTIGATED USING GUINEA PIGS AS AN ANIMAL MODEL. **TOLUENE** DIISOCYANATE (1-100% CONCN) WAS APPLIED TO DORSAL SITES ON GUINEA PIGS, WHERE SKIN SENSITIVITY TO TDI WAS APPARENT BY THE 7TH DAY. AFTER 14 DAYS, ANIMALS WERE ADDNL EVALUATED FOR TDI SENSITIVITY BY SEROLOGIC ANALYSIS & BRONCHIAL PROVOCATION CHALLENGE. ANTIBODIES TO **TOLUENE** DIISOCYANATE WERE DETECTED USING PASSIVE CUTANEOUS ANAPHYLAXIS, DOUBLE DIFFUSION IN GEL, & RADIOLABELED ANTIGEN BINDING ASSAYS. ANTIBODIES WERE SPECIFIC FOR **TOLUENE** DIISOCYANATE. THE DEVELOPMENT OF RESPIRATORY HYPERSENSITIVITY AS A RESULT OF DERMAL CONTACT WITH **TOLUENE** DIISOCYANATE EMPHASIZES THE IMPORTANCE OF CAREFUL WORKPLACE PRACTICES & SUGGESTS REEVALUATION OF THE ROLE OF INHALATION &/OR DERMAL CONTACT IN CAUSING PULMONARY SENSITIZATION OF WORKERS.
[KAROL MH ET AL; TOXICOL APPL PHARMACOL 58 (2): 221 (1981)]**PEER REVIEWED**

TOLUENE DIISOCYANATE WAS MUTAGENIC IN SALMONELLA TYPHIMURIUM STRAINS TA1538 & TA98 AFTER METABOLIC ACTIVATION.
[ANDERSEN M ET AL; SCAND J WORK ENVIRON HEALTH 6 (3): 221 (1980)]**PEER REVIEWED**

GROUPS OF MALE & FEMALE RATS & MICE WERE EXPOSED TO 0.05 & 0.15 PPM OF 2,4/2,6-**TOLUENE**-DIISOCYANATE (80/20) BY INHALATION FOR 6 HR/DAY, 5 DAYS/WEEK FOR 2 YR. TYPE & INCIDENCE OF TUMORS & THE NUMBER OF TUMOR-BEARING ANIMALS OF EITHER SPECIES DID NOT INDICATE ANY CARCINOGENIC EFFECT. HEMATOLOGY, BIOCHEMISTRY, URINALYSIS, & CYTOGENICITY STUDIES DID NOT REVEAL ANY UNTOWARD EFFECT. INCREASED MORTALITY (FEMALES ONLY), REDUCED WEIGHT GAIN & SIGNS OF IRRITATION IN THE UPPER & LOWER RESPIRATORY TRACT RESULTED FROM EXPOSURE TO **TOLUENE** DIISOCYANATE IN THE MOUSE STUDY WITH THE HIGHEST INCIDENCE IN THE 0.15 PPM EXPOSURE LEVEL.
[LOESER E; TOXICOL LETT (AMST) 71 (1983)]**PEER REVIEWED**

EXPOSURE BY INHALATION TO 70 MG/CU M (10 PPM) ... 2,6-TDI OR 65/35 MIXT FOR 6 HR/DAY FOR 3-5 DAYS WAS LETHAL TO RATS; EXPOSURE TO 35 MG/CU M (5 PPM) OF MIXT FOR 4 DAYS KILLED 65% OF RATS.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V19 310 (1979)]**PEER REVIEWED**

LC50 FOLLOWING EXPOSURE ... FOR 14 DAYS WAS: MOUSE, 70 MG/CU M ... GUINEA PIG, 90 MG/CU M ... & RAT, 100 MG/CU M ... LC50 FOLLOWING EXPOSURE FOR 7 DAYS WAS 80

MG/CU M ... IN RABBITS. ... MICE, RATS & GUINEA PIGS EXHIBITED LACRIMATION, SALIVATION, RESTLESSNESS & HYPERACTIVITY.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V19 310 (1979)]**PEER REVIEWED**

ACUTE 6-HR INHALATION STUDIES IN RATS, CONCN OF 4200 MG/CU M ... WAS LETHAL, WHEREAS 420 MG/CU M ... WAS NOT. ANIMALS THAT DIED SHOWED ACUTE PULMONARY CONGESTION & EDEMA.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V19 310 (1979)]**PEER REVIEWED**

FOLLOWING EXPOSURE BY INHALATION ... TO 0.7 MG/CU M (0.1 PPM) ... FOR 6-HR ... 1 DAY/WK FOR 38 WK, OR ... 6 HR/DAY ON 5 DAYS/WK FOR ... 58 EXPOSURES, RAT SHOWED PROLIFERATION OF FIBROUS TISSUE ... OF BRONCHIOLES AS WELL AS PNEUMONITIS, TRACHEITIS & BRONCHITIS. IN RABBITS & GUINEA PIGS, NO PROLIFERATION ... .
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V19 310 (1979)]**PEER REVIEWED**

ACUTE SKIN ABSORPTION TESTS ... ON RABBITS PRODUCED SEVERE LOCAL IRRITATION BUT FAILED TO KILL, EVEN WITH DOSES AS HIGH AS 16 G/KG BODY WT ... NO ANATOMICAL INJURY TO INTESTINAL ORGANS.
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TEST APPLICATION OF DROP OF META & PARA TOLUENEDIISOCYANATES ON RABBIT EYES CAUSED IMMEDIATE PAIN, LACRIMATION, SWELLING OF LIDS, & CONJUNCTIVAL REACTION. HOWEVER, CORNEAL EPITHELIUM WAS ONLY MILDLY DAMAGED ... /MIXT OF 2,4- & 2,6-ISOMERS/
[Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986. 929]**PEER REVIEWED**

EXPOSURE OF GUINEA PIGS BY INHALATION TO 14-35 MG/CU M (2-5 PPM) ... IN AIR ... 6 HR/DAY FOR 3 DAYS RENDERED THEM MORE SENSITIVE WHEN 3 WK LATER THEY WERE EXPOSED TO 0.14 MG/CU M (0.02 PPM) FOR 5 HR, AS SHOWN BY MORE PRONOUNCED REDN OF BREATH RATE ... COMPARED WITH ANIMALS ... NOT ... PREVIOUSLY EXPOSED.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V19 310 (1979)]**PEER REVIEWED**

Groups of 120 male and 120 female CD-1 mice, three to four weeks old, were exposed to 0, 0.05, or 0.15 ppm (0, 0.36 or 1.07 mg/cu m) production grade **toluene** diisocyanate (approx 80% 2,4 isomer & 20% 2,6 isomer) in an inhalation chamber for 6 hr/day on 5 days/wk for 104 wk. There was a significant reduction in body weight in the high-dose group /sex not stated/ and a significant increase in mortality in both high and low-dose females by the termination of the study. No such effect was seen in males. Neither the types of tumor observed nor their incidences were dose-related, and both corresponded to those seen in historical controls for this strain of mice. However, dose-related pathological changes were observed in the nasal cavity (chronic or necrotic rhinitis), together with changes in the lower respiratory tract (interstitial pneumonia, catarrhal bronchitis) in both groups.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 303 (1986)]**PEER REVIEWED**

Groups of 126 male and 126 female Sprague Dawley CD rats, six to nine weeks old, were exposed to 0, 0.05 or 0.15 ppm (0, 0.36 or 1.07 mg/cu m) production-grade **toluene** diisocyanate (approx 80% 2,4 isomer and 20% 2,6 isomer) in an inhalation chamber for 6 hr/day on 5 days/wk for 108 wk or 110 wk. A significant reduction in weight gain was observed during the first 12 wk of the study among the high-dose animals of each sex, but body wt gain was similar in all groups thereafter. No significant difference in mortality between treated and control groups of either sex was reported. Tumor incidences and types were reported to be similar in control and treated groups.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 304 (1986)]**PEER REVIEWED**

Rats receiving up to 240 mg/kg **toluene** diisocyanate by gavage daily on 5 days/wk for 13 wk were found to suffer from mild to moderate bronchopneumonia.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 306 (1986)]**PEER REVIEWED**

In dogs, a correlation has been made between immunological and respiratory responses to **toluene** diisocyanate. Dogs exposed once every second week for 41 wk to 1 mg/kg **toluene** diisocyanate delivered as an aerosol intratracheally developed a systemic immune response to **toluene** diisocyanate conjugated with dog serum albumin as well as immediate-type airway responses.
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The **toluene** diisocyanate induced delayed type hypersensitivity reaction in the ear of male mice was investigated and compared with the picryl chloride induced one. The results obtained were as follows: 1) When 1% **toluene** diisocyanate solution (20 ul/ear) as a challenging concentration was used for 7 week old ICR mice, distinct ear swelling was observed in every group sensitized with various concentrations (1-5%, 100 ul/animal) of **toluene** diisocyanate solution, and the swelling rate was the same or higher than

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[Thompson JE et al; Am Rev Respir Dis 136 (1): 43-9 (1987)]**PEER REVIEWED**

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[Gordon T et al; Am Rev Respir Dis 132 (5): 1106-12 (1985)]**PEER REVIEWED**

The effect of exposure to **toluene** diisocyanate vapor on pulmonary performance was studied in guinea pigs. Female English smooth haired guinea pigs were exposed to 1.4 ppm **toluene** diisocyanate vapor or air for 3 hours per day for 4 days, or to 0.02 ppm **toluene** diisocyanate for 6 hours per day for 70 days. Pulmonary performance was evaluated by the ventilatory response of the animals to 10% carbon dioxide. Serum antibodies to **toluene** diisocyanate were measured on days 22 and 50 and **toluene** diisocyanate pulmonary hypersensitivity was measured on days 37 and 38. Lung tissue histopathology was evaluated in all animals on day 50 following **toluene** diisocyanate exposure. Pulmonary response to 10% carbon dioxide diminished by 30 to 50% following **toluene** diisocyanate exposures at 1.4 ppm up to day 14. The ventilatory response showed recovery during the next 5 weeks. In contrast, animals exposed to 0.02 ppm **toluene** diisocyanate daily for 70 days showed no change in ventilatory response, nor did control animals that were not exposed to **toluene** diisocyanate. Antibodies were detected on day 22 and pulmonary hyprsensitivity to **toluene** diisocyanate was found in all animals exposed to 1.4 ppm **toluene** diisocyanate. No antibodies to **toluene** diisocyanate nor pulmonary hypersensitivity were detected in animals exposed to 0.02 ppm **toluene** diisocyanate or in control animals. Lung tissue on day 50 in the 1.4 ppm **toluene** diisocyanate exposed animals showed multifocal subchronic interstitial inflammation, localized pleural thickening, and peripheral lymphoid hyperplasia. No apparent abnormalities were observed in lung tissue of the 0.02 ppm exposed group. Exposure to 1.4 or 0.02 ppm **toluene** diisocyanate resulted in measurable and no apparent pulmonary toxicity in guinea pigs, respectively. The 10 percent carbon dioxide challenge provide several advantages for measuring pulmonary function.
[Wang KL et al; J Toxicol Environ Health 15 (1): 137-48 (1985)]**PEER REVIEWED**

Groups of 50 F344/N rats of each sex and 50 B6C3F1 mice of each sex were gavaged with corn oil or a mixture of **toluene** diisocyanate in corn oil for 5 days per wk for 105 or 106 wk. Female rats and mice were given doses of 60 or 120 mg/kg body weight, while male rats received 30 or 60 mg/kg, and male mice received 120 or 240 mg/kg. The **toluene** diisocyanate reacted with the moisture in the corn oil vehicle resulting in doses that were 10% to 23% below the target dose concn. The chemical product used was commercial grade **toluene** diisocyanate, which was an 80%-20% mixture of the 2,4- and 2,6-isomers. Chemical disposition and metabolism studies were conducted with each of the radiolabelled **toluene** diisocyanate isomers in male rats. Absorption of both of the **toluene** diisocyanate isomers occurred, with the highest concn found in the stomach, cecum, large intestine, and bladder. Excretion occurred via the feces and urine. The major metabolic products from the metabolism of 2,4-**toluene** diisocyanate were shown to be identical with those from the metabolism of the carcinogen, 2,4-diaminotoluene, whereas the metabolism of the 2,6-**toluene** diisocyanate isomer yielded one major product, identified as 2,6-bis(acetylamino)**toluene**. Greater than 10% depression in body weight gain occurred in all dosed groups of rats throughout most of the study. The major non-neoplastic lesions that

were observed in both sexes of the **toluene** diisocyanate exposed rats were dose related incr in acute broncho-pneumonia, characterized as chemical pneumonitis, with incidences as high as 50%. In mice mean body weight gain was depressed in dosed male and in high dose females. The principle non-neoplastic lesion in mice that was attributed to chemical treatment was cytomegaly of the kidney tubular epithelium in males. Survival in all groups of dosed rats was significantly lower than in controls. A dose-dependent pattern of mortality did not commence until 70 wk of exposure, demonstrating that **toluene** diisocyanate elicited a cumulative toxic response. There was also significantly lower survival in high dose male, but not female mice, by comparison to controls. Despite the reduction of power and sensitivity in the rat studies caused by early mortality, statistically significant incr in tumor incidences were observed in many different target organs. **Toluene** diisocyanate was carcinogenic in F344/N rats, causing sc fibromas and fibrosarcomas in males and females, pancreatic acinar cell adenomas in males, and pancreatic islet cell adenomas, neoplastic nodules of the liver, and mammary gland tumors in females.
[Dieter MP et al; Toxicol Ind Health 6 (6): 599-621 (1990)]**PEER REVIEWED**

Toluene diisocyanate is a causative agent in occupational asthma. Through an oral catheter **toluene** diisocyanate, 0.03 ul, dissolved in 0.02 ml olive oil, was superfused on the tracheobronchial mucosa of anaesthetized guinea pigs. **Toluene** diisocyanate induced plasma exudation into both airway tissue and lumen (peak effect: 5 hr; duration approximately 17 hr). Light microscopy examinations demonstrated that the epithelium was not disrupted by this process (and that microvessels are abundant just beneath the epithelium). At days 6 and 21 after exposure to **toluene** diisocyanate PAS-positive cells were increased, but no other histological alterations were found. Also, the occurrence of peptide containing nerve fibres was not altered by **toluene** diisocyanate. After **toluene** diisocyanate exposure the airway smooth muscle tone was elevated as examined in vitro at base-line and at conc response to carbachol. The largest incr in tone were recorded 21 days after exposure to **toluene** diisocyanate. The abnormally large tone was not associated with an increased thickness of the smooth muscle layer nor was it associated with reduced effects of either beta 2-agonist (terbutaline) or xanthine (theophylline) relaxants. It is concluded that **toluene** diisocyanate induced plasma exudation into guinea pig airways for 17 hr without disrupting the epithelial lining and without causing major changes in the airway peptidergic innervation. Both the airway tone, and the number of mucous cells, are increased for at least 3 wk after exposure to **toluene** diisocyanate.
[Persson CG et al; Clin Exp Allergy 21 (6): 715-24 (1991)]**PEER REVIEWED**

Toluene diisocyanate was mutagenic in Salmonella typhimurium strains TA98 and TA100 in the presence (but not the absence) of Aroclor 1254-induced male Sprague Dawley rat or male Syrian hamster liver S9; it was not mutagenic in strains TA 1535 or 1537.
[DHHS/NTP; Toxicology and Carcinogenesis Studies of Commercial Grade 2,4 (80%) and 2,6 (20%) - Toluene Diisocyanate (Gavage Studies) p. 7 (1986) Technical Rpt Series No. 251 NIH Pub No. 86-2507]**PEER REVIEWED**

TOLUENE DIISOCYANATE

CASRN: 26471-62-5

For other data, click on the Table of Contents

Non-Human Toxicity Values:

LC50 Rat inhalation 56.96 mg/cu m/1 hr
[WHO; Environmental Health Criteria 75: Toluene Diisocyanates p. 33 (1987)]**PEER REVIEWED**

LC50 Rat inhalation 98.96 + or - 8.6 mg/cu m/4 hr
[WHO; Environmental Health Criteria 75: Toluene Diisocyanates p. 33 (1987)]**PEER REVIEWED**

LC50 Rat (male) inhalation 348.88 mg/cu m/4 hr
[WHO; Environmental Health Criteria 75: Toluene Diisocyanates p. 33 (1987)]**PEER REVIEWED**

LC50 Rat (female) inhalation 356 mg/cu m/4 hr
[WHO; Environmental Health Criteria 75: Toluene Diisocyanates p. 33 (1987)]**PEER REVIEWED**

LC50 Mouse inhalation 69.1 + or - 9.96 mg/cu m/4 hr
[WHO; Environmental Health Criteria 75: Toluene Diisocyanates p. 33 (1987)]**PEER REVIEWED**

LC50 Rabbit inhalation 78.32 mg/cu m/4 hr
[WHO; Environmental Health Criteria 75: Toluene Diisocyanates p. 33 (1987)]**PEER REVIEWED**

LC50 Guinea pig inhalation 90.4 + or - 19.2 mg/cu m/4 hr
[WHO; Environmental Health Criteria 75: Toluene Diisocyanates p. 33 (1987)]**PEER REVIEWED**

LD50 Rat oral 3060 mg/kg
[WHO; Environmental Health Criteria 75: Toluene Diisocyanates p. 33 (1987)]**PEER REVIEWED**

TOLUENE DIISOCYANATE

CASRN: 26471-62-5

For other data, click on the Table of Contents

Metabolism/Pharmacokinetics:

Metabolism/Metabolites:

A technique for detectingurinary amine metabolites in rats exposed to **toluene** diisocyanate was evaluated. Skin tissue of rats was exposed to 40% **toluene**-2,4-diisocyanate solution in di-n-butyl-ether liquid. Rats were exposed daily for 3 hr on 4 consecutive days. Urine was collected in metabolic cages for 18 hr after the last exposure. Chromatographic techniques were used for nitrogen selective detection of nonderivatized amines. An autolinear temperature programmer was employed to analyze derivatized amine. The identity of the amine was confirmed by gas chromatography/mass spectrometry. A linear correlation was found between **toluene**-2,4-diamine added to urine and peak height. Peak height and recovery from the non hydrolyzed and from the hydrolyzed urine was about 85 and 70%, respectively. No free **toluene**-2,4-diamine or free **toluene**-2,4-diisocyanate was detected in the urine of rats exposed to **toluene**-2,4-diamine in hydrolyzed urine was 1.5 micrograms per milliliter. Gas chromatography/mass spectrometry confirmed the identity of the amine. /This/ highly sensitive technique tested is easy to apply and is effective for trace assays of amines.
[Rosenberg C; J Chromatography 323 (2): 429-33 (1985)]**PEER REVIEWED**

Epithelial injury and inflammation are involved in airway hyperresponsiveness and asthma induced by **toluene** diisocyanate. In that isocyanates are insoluble and highly reactive compounds, bronchial epithelial cells may represent the most important target cells of their toxic effect. We hypothesized that damage to airway epithelium by **toluene** diisocyanate may result in the release of metabolites of arachidonic acid, which are known to promote inflammation and to alter epithelial cell function and airway smooth muscle responsiveness. To test this hypothesis we examined eicosanoid products in the culture media of bronchial epithelial cells exposed in vitro to 8 and 18 ppb **toluene** diisocyanate. Epithelial cells derived from human bronchi obtained at surgery were cultured to confluency on collagen-coated microporous membranes. Those cells, which expressed differentiated characteristics of epithelial cells (they showed keratin-containing filaments and had a cobblestone appearance), were alternatively exposed to **toluene** diisocyanate or air for 30 min in a specially designed in vitro chamber. The production of metabolites of arachidonic acid was assessed by measuring the release of immunoreactive products into the cell medium at the end of the exposure and during a 2 hr period after exposure. This method revealed a predominant isocyanate induced release of immunoreactive 15-hydroxyeicosatetraenoic acid. Release rate of this compound tended to be dose-related and was associated with cell damage as assessed by the release of lactate dehydrogenase in the medium.
[Mattoli S et al; J Cell Physiol 142 (2): 379-85 (1990)]**PEER REVIEWED**

It has been previously shown that tachykinin depletion or antagonism prevented the increase in airway responsiveness to inhaled acetylcholine caused by exposure to **toluene** diisocyanate in awake guinea pigs. To insure that the effects of tachykinins were not limited to the extrathoracic airways and were not dependent on effects of **toluene** diisocyanate on baseline airway caliber, airway responsiveness to acetylcholine inhaled through tracheostomy in anesthetized and ventilated guinea pigs that were exposed

to **toluene** diisocyanate or air after treatment with the tachykinin antagonist spantide, the tachykinin metabolism inhibitor phosphoramidon, or the vehicles for each drug were determined. When these drugs were administered before and during **toluene** diisocyanate exposure, spantide significantly inhibited the **toluene** diisocyanate induced increase in acetylcholine responsiveness and phosphoramidon significantly potentiated this effect, whereas neither drug altered acetylcholine responsiveness in air exposed animals. To determine whether tachykinins were exerting their effect primarily during **toluene** diisocyanate exposure or during the subsequent acetylcholine challenge, the effect of each drug on acetylcholine responsiveness was also examined when the drugs were given after **toluene** diisocyanate exposure. At that time, spantide did not inhibit **toluene** diisocyanate induced acetylcholine hyperresponsiveness and phosphoramidon did not potentiate it. Neither drug nor **toluene** diisocyanate increased pulmonary resistance measured through a tracheostomy in these anesthetized and ventilated animals. These results suggest that the **toluene** diisocyanate induced increase in acetylcholine responsiveness is mediated by release of tachykinins into the intrathoracic airways during exposure to **toluene** diisocyanate.
[Sheppard D, Scypinski L; Am Rev Respir Dis 138 (3): 547-51 (1988)]**PEER REVIEWED**

Five men were exposed to **toluene** diisocyanate atmospheres for 7.5 hr. The **toluene** diisocyanate atmospheres were generated by a gas-phase permeation method, and the exposures were performed in an 8 cu m stainless steel test chamber. The mean air concn of **toluene** diisocyanate was ca 40 ug/cu m, which corresponds to the TLV of Sweden. The inhaled doses of 2,4- and 2,6-**toluene** diisocyanate were ca 120 ug. **Toluene** diisocyanate in the test chamber air was determined by an HPLC method using the 9-(N-methylaminomethyl)-anthracene reagent and by a continuous monitoring filter-tape instrument. After hydrolysis of plasma and urine, the related amines, 2,4- and 2,6-toluenediamine 2,4-, and 2,6-TDA), were determined as pentafluoropropionic anhydride derivatives by capillary gas-chromatography using selected ion monitoring in the electron-impact mode. The urinary elimination of the toluenediamines showed a possible biphasic pattern, with rapid first phases for 2,4-toluenediamine (mean half-life for the concn in urine, 1.9 hr) and for 2,6-toluenediamine (mean half-life for the concn in urine, 1.6 hr). The cumulative amount of 2,4-toluenediamine excreted in urine within 28 hr ranged from 8% to 14% of the estimated dose of 2,4-**toluene** diisocyanate, and the cumulative amount of 2,6-toluenediamine in urine ranged from 14% to 18% of the 2,6-**toluene** diisocyanate dose. The average urinary level of 2,4-toluenediamine was 5 ug/l in the 6 to 8 hr sample (range 2.8-9.6 ug/l), and the corresponding value fo 2,6-toluenediamine was 8.6 ug/l (range, 5.6-16.6 ug/l). Biological monitoring of exposure to 2,4- and 2,6-**toluene** diisocyanate by analysis of 2,4- and 2,6-toluenediamine in urine is feasible.
[Skarping G et al; Int Arch Occup Environ Health 63 (2): 83-8 (1991)]**PEER REVIEWED**

Mechanism of Action:

SERUM FROM 26 PERSONS SHOWN TO REACT TO PROVOCATIVE INHALATION CHALLENGE WITH LOW CONCN OF **TOLUENE** DIISOCYANATE WAS TESTED BY RADIOALLERGOSORBENT TEST (RAST) USING A P-TOLYL ISOCYANATE-HUMAN SERUM ALBUMIN (TMI-HSA) CONJUGATE. POSITIVE RESULTS WERE OBTAINED IN 15-19% OF **TOLUENE** DIISOCYANATE REACTORS, DEPENDING ON THE METHOD OF EVALUTION. **TOLUENE** DIISOCYANATE ASTHMA MAY BE A COMPLEX SYNDROME WITH SEVERAL TYPES OF REACTIONS POSSIBLE, INCLUDING AN IMMUNOGLOBULIN-E MECHANISM IN SOME INDIVIDUALS. THE THEORY THAT **TOLUENE** DIISOCYANATE ASTHMA IS BASED

SOLELY ON AN IMMUNE MECHANISM IS NOT SUPPORTED. THE FINDINGS DO NOT DISAGREE WITH THE HYPOTHESIS THAT **TOLUENE** DIISOCYANATE REACTIVITY MAY BE MEDIATED BY A PHARMACOLOGIC MECHANISM.
[BUTCHER BT ET AL; J ALLERGY CLIN IMMUNOL 66 (3): 213 (1980)]**PEER REVIEWED**

To investigate the role of pharmacological mechanisms in **toluene** diisocyanate induced occupational asthma, the effects of **toluene** diisocyanate on rat trachea ring and lung parenchymal strip were studied in vitro. The most prominent effect observed was a stimulation of metacholine induced contraction of the tracheal ring by 1M **toluene** diisocyanate (added in dimethyl sulfoxide). The results were less pronounced when **toluene** diisocyanate was added from a stock solution prepared in water, which is possibly due to copolymerisation. It is concluded that the pharmacological effect of **toluene** diisocyanate may result from an autonomic imbalance between cholinergic and B-adrenergic neural control.
[Borm PJA et al; Br J Ind Med 46 (1): 56-9 (1989)]**PEER REVIEWED**

A study of the occurrence of serum immunoglobulin-E and immunoglobulin-G antibodies in workers with isocyanate induced asthma was conducted. The study group consisted of 62 workers (58 males) being evaluated for occupational asthma. Thirty nine had been exposed to hexamethylene diisocyanate, 17 to diphenylmethane diisocyanate, and six to **toluene** diisocyanate. The subjects completed a respiratory and occupational questionnaire. Spirometric tests were administered. Skin prick tests were performed with 15 common inhalant allergens and **toluene** diisocyanate, hexamethylene diisocyanate, and diphenylmethane diisocyanate human serum albumin conjugates. Blood samples were collected and assayed for specific serum immunoglobulin-G and immunoglobulin-E antibodies to hexamethylene diisocyanate, diphenylmethan diisocyanate, and **toluene** diisocyanate. Specific inhalation challenges were conducted with hexamethylene diisocyanate, diphenylmethane diisocyanate, and **toluene** diisocyanate. Specific inhalation challenge with **toluene** diisocyanate, hexamethylene diisocyanate, or diphenylmethane diisocyanate induced significant bronchoconstriction in half of the subjects, late reactions being the most common. Twenty subjects had significantly elevated immunoglobulin-G concn and nine had significantly elevated immunoglobulin-G plus immunoglobulin-E concn. Six of 12 subjects with elevated immunoglobulin-E and immunoglobulin-G antibodies had positive skin prick tests for hexamethylene diisocyanate and one was sensitized to diphenylmethane diisocyanate. It was concluded that an association between isocyanate specific antibodies and the results of specific inhalation challenge tests has been established. This suggests that isocyanate induced asthma may involve an immunological mechanism.
[Cartier A et al; J Allergy Clin Immunol 84 (4 Part 1): 507-14 (1989)]**PEER REVIEWED**

The influence of cyclophosphamide induced granulocyte depletion on **toluene** diisocyanate related changes in airway reactivity and pathology was assessed in guinea pigs. Twelve cyclophosphamide-treated and 12 control animals comprising each group were studied physiologically before and 2 hr after a single 10 min exposure to 3 ppm of **toluene** diisocyanate. Reactivity was determined in intact unanesthetized animals by measuring specific airway conductance before and during intravenous acetylcholine infusion. After testing, tracheal tissue for light microscopic examination was obtained from three hyperreactive guinea pigs in each exposed group and compared with tissue from treated and control animals (n = 3 each) that had not been **toluene** diisocyanate exposed. Cyclophosphamide treatment caused substantial decr in both circulating and airway granulocyte counts. However, the incidence and degree of bronchial hyperreactivity that occurred 2 hr post-**toluene**

diisocyanate was similar in the untreated and treated groups. Results indicate that **toluene** diisocyanate induced bronchial hyperreactivity 1) occurs shortly after a brief high concn exposure and 2) appears independent of circulating or airway granulocyte counts.
[Cibulas W Jr et al; J Appl Physiol 64 (5): 1773-8 (1988)]**PEER REVIEWED**

To determine the importance of airway inflammation for the development of late asthmatic reactions, we examined sensitized subjects during late asthmatic reactions induced by exposure to **toluene** diisocyanate in the laboratory. Late asthmatic reactions are associated with a transient increase of bronchial responsiveness and, at the same time, with an increase of neutrophils followed by eosinophils, and of leukotriene B4 and albumin in bronchoalveolar lavage fluid. Late asthmatic reactions, increased bronchial responsiveness, and increase of neutrophils, eosinophils, leukotriene B4, and albumin concn in bronchoalveolar lavage induced by exposure to **toluene** diisocyanate are all prevented by pretreatment with prednisone but not with the nonsteroidal anti-inflammatory agent indomethacin. Aerosolized steroids (beclomethasone and dexamethasone isonicotinate) completely inhibit late asthmatic reactions induced by **toluene** diisocyanate, whereas theophylline has a partial, and verapamil, ketotifen, and cromolyn have no protective effect. These results suggest that late asthmatic reactions induced by **toluene** diisocyanate may be caused by airway inflammation, and that anti-inflammatory steroids should be recommended in the prophylaxis of **toluene** diisocyanate asthma.
[Fabbri LM et al; Am Rev Respir Dis 143 (3 Pt 2): 537-8 (1991)]**PEER REVIEWED**

The effects of **toluene** diisocyanate on T-cell subpopulations and circulating lymphocytes in ten persons (five males)): 19 to 50 yr old, with **toluene** diisocyanate induced occupational asthma were examined. Five subjects revealed early and late asthmatic reactions to **toluene** diisocyanate (dual responders) and five revealed late asthmatic reactions (late responders). Subjects underwent inhalation challenge with 0.005 to 0.015 ppm **toluene** diisocyanate or filtered air for 10 to 30 min on two occasions. One second forced expiratory volumes were measured before and at periodic intervals between 30 min and 24 hr after challenge. Venous blood samples were drawn 30 min and 8, 24, 48, and 72 hr after **toluene** diisocyanate. Total and differential leukocyte counts and T-cell subpopulations were determined. The five dual responders demonstrated forced expiratory volume in 1 sec decreased indicative of early and late asthmatic reactions and the five late responders demonstrated forced expiratory volume in 1 second decr indicative of a late asthmatic reaction. **Toluene** diisocyanate challenge did not affect the number of circulating erythrocytes and leukocytes. The percentage of eosinophils was significantly increased 24 hr after challenge and sustained for up to 48 hr. The percentages of neutrophils, lymphocytes, and monocytes were not altered by **toluene** diisocyanate. Among the T-lymphocyte subpopulation, the proportion of CD8(+) lymphocytes was significantly increased 8 hr after **toluene** diisocyanate challenge. The increase was more pronounced in the lat responders. An additional increase in CD8(+) lymphocytes occurred 48 hr post exposure in seven subjects but was unrelated to responder type. The number of CD4(+) cells did not change. This resulted in a decrease in the CD4(+)/CD8(+) ratio 8 and 48 hr after **toluene** diisocyanate challenge. It was concluded that **toluene** diisocyanate induced late asthmatic reactions are associated with an increase in the number of suppressor/cytotoxic lymphocytes and eosinophils in peripheral blood.
[Finotto S et al; Br J Ind Med 48 (2):116-21 (1991)]**PEER REVIEWED**

Intravenously administered endotoxin inhibits the polymorphonuclear leukocyte dependent airway edema produced in guinea pigs exposed to **toluene** diisocyanate. Tumor necrosis factor is produced in

vivo by peripheral blood monocytes and tissue macrophages stimulated with endotoxin and has been shown to activate polymorphonuclear leukocyte's and vascular endothelial cells. To determine whether the inhibition of airway edema is mediated by tumor necrosis factor, guinea pigs were treated with intravenous saline or 75,000 U/kg recombinant human tumor necrosis factor 1.5 hr before exposure to air or 3 ppm **toluene** diisocyanate for 1 hr. Animals were then injected intravenously with 50 mg/kg Evans blue dye as a marker of protein extravasation. Saline-treated animals exposed to **toluene** diisocyanate had a significant increase in tracheal Evans blue dye extravasation (85 + or - 6.5 ug dye/g trachea, mean + or - standard error) compared with saline-treated animals exposed to air (31.3 + or - 2.5, $P < 0.001$). The tracheal extravasation of Evans blue dye was significantly inhibited ($P < 0.05$) in **toluene** diisocyanate exposed animals treated with tumor necrosis factor (64.7 + or - 7.5). Neither heat-inactivated tumor necrosis factor (104.9 + or - 9.5) nor tumor necrosis factor neutralized with a monoclonal antibody against tumor necrosis factor (99.7 + or - 17.9) inhibited **toluene** diisocyanate induced airway edema. In addition, treatment with 15,000 U/kg (99.9 + or - 21.3) or 150,000 U/kg (103.2 + or - 17.6) interleukin 1, a monokine also produced in response to endotoxin, did not prevent airway edema. These results suggest that tumor necrosis factor released in response to endotoxin mediates endotoxin's inhibition of a polymorphonuclear leukocyte dependent airway edema.
[Gordon T, Sheppard D; J Appl Physiol 64 (4): 1988 1688-92]**PEER REVIEWED**

Serum immunoglobulin-G and immunoglobulin-E to isocyanate haptenized human serum albumin (HSA) were estimated by ELISA in 55 isocyanate workers who underwent isocyanate inhalation challenge studies in Montreal, Canada. The challenges were negative in 29 workers and positive in 26 workers. Isocyanate antibodies were estimated by ELISA index. The mean immunoglobulin-G indices were found to be significantly higher in the challenge-positive workers, and there was a similar trend for the immunoglobulin-E indices. Antibody specificities for **toluene** diisocyanate-human serum albumin, diphenylmethane diisocyanate-human serum albumin, and hexamethylene diisocyanate-human serum albumin were determined by inhibition studies with a variety of isocyanate haptenized carriers. The other isocyanate substituted carriers were either noninhibitory or caused only partial inhibition as contrasted with the complete inhibition achieved by human serum albumin conjugated to the isocyanate to which the worker was exposed. We interpret these specificity studies as indicating that the inhalation of isocyanates results in production of antibody that recognizes new antigenic determinants that develop from the coupling of isocyanates to homologous proteins.
[Grammer LC et al; J Allergy Clin Immunol 86 (1): 94-8 (1990)]**PEER REVIEWED**

Inhalation of **toluene** diisocyanate results in toxic responses ranging from pulmonary irritation to immunological sensitization. The use of radioactively labeled isocyanate has made it possible to follow the initial uptake of the compound into the bloodstream independent of the final fate of the isocyanate. This study shows that the rate of uptake into the blood is linear during exposure to concn ranging from 0.00005 to 0.146 ppm and that the uptake continues to increase slightly postexposure. It also demonstrates that the radioactivity clears from the bloodstream to a level corresponding to approximately a 100 nM concn of tolyl group after 72 hr and persists at a nanomolar level even 2 wk following the exposure. The initial rate of (14)C uptake is also a linear function of the concn of **toluene** diisocyanate when expressed either as concn (ppm) or as concn multiplied by duration of exposure (ppm.hr). This is discussed in comparison with the toxic responses as a function of both ppm and ppm.hr. Finally, the inclusion of the data on methyl isocyanate indicates that the uptake into arterial blood is a function of

exposure concn, independent of isocyanate structure.
[Kennedy AL et al; Toxicol Appl Pharmacol 100 (2): 280-92 (1989)]**PEER REVIEWED**

Isocyanates are an important cause of occupational asthma. The mechanism of isocyanate induced asthma is still unknown. To determine whether **toluene** diisocyanate stimulates the 'efferent' function of peripheral endings of capsaicin-sensitive sensory nerves, we investigated the effect of **toluene** diisocyanate in the rat isolated urinary bladder, a preparation in which the action of capsaicin has been well characterized. **Toluene** diisocyanate (0.03 mM) produced a concn dependent contraction of the bladder strips. It maximal effect was about 50 % of the response to capsaicin (1 uM). Previous exposure of the strips to capsaicin followed by washing out produced complete unresponsiveness, both to the first exposure to **toluene** diisocyanate and to a second exposure of capsaicin. Further, the response to both **toluene** diisocyanate and capsaicin was completely prevented by extrinsic bladder denervation, achieved by bilateral removal of pelvic ganglia (72 hr before). Repeated exposure of the rat bladder to **toluene** diisocyanate reduced the capsaicin-evoked release of calcitonin gene-related peptide like immunoreactivity (CGRP-LI), taken as biochemical marker of activation of these sensory nerves. These experiments provide the first evidence that **toluene** diisocyanate activates directly or indirectly the efferent function of capsaicin-sensitive primary sensory nerves.
[Mapp CE et al; Eur J Pharmacol 180 (1): 113-8 (1990)]**PEER REVIEWED**

The in vivo exposure to an asthmogenic stimulus, **toluene** diisocyanate, causes airway epithelial damage associated with inflammation and increased bronchial hyperresponsiveness. The latter mechanisms might partly be mediated by the release of eicosanoids from bronchial epithelial cells. Previously it has been demonstrated that the in vitro exposure of bronchial epithelial cells to **toluene** diisocyanate results in the release of immunoreactive 15-hydroxyeicosatetraenoic acid, a product of activation of the 15-lipoxygenase pathway with inflammatory properties. Present study shows that **toluene** diisocyanate induced release of 15-hydroxyeicosatetraenoic acid from epithelial cells can be prevented by nedocromil sodium, an anti-asthmatic drug with anti-inflammatory properties. This mode of action of the compound may explain its clinical effectiveness in asthma.
[Mattoli S et al; Int Arch Allergy Appl Immunol 92 (1): 16-22 (1990)]**PEER REVIEWED**

To determine whether early and/or late asthmatic responses induced by **toluene** diisocyanate are caused by a reflex mechanism involving stimulation of muscarinic receptors, we studied the effect of the muscarinic antagonist atropine on early and late airway response induced by **toluene** diisocyanate. A preliminary study was conducted in asthmatics to assess whether the selected dose of atropine provided adequate muscarinic blockade. On different days we measured the provocation dose (in mg) of carbachol causing a 15% decrease in forced expiratory volume in 1 second (PD15FEV1) without and with atropine premedication (0.008 or 0.012 mg/kg sc atropine 30 or 90 min before carbachol challenge test). 0.008 to 0.012 mg/kg sc atropine increased the PD15FEV1 carbachol by 6 to 10 fold, inducing a consistent and prolonged decrease in nonspecific bronchial hyperresponsiveness to cholinergic agent. 10 Subjects with a history of sensitization to **toluene** diisocyanate were then examined in 2 sets of experiments. In the first set of experiments, the subjects were studied before and after exposure to **toluene** diisocyanate (0.04 ppm; 30 min) after no treatment. In the second set of experiments, carried out 1 to 2 wk later, the same procedure was repeated after treatment with atropine (0.008 to 0.012 mg/kg atropine sulfate administered sc 30 min before **toluene** diisocyanate challenge, and then at 90 min intervals after **toluene** diisocyanate

exposure); all patients showed symptoms of atropine effect (dryness of mouth, cycloplegia, increased heart rate).
[Paggiaro P et al; Am Rev Respir Dis 136 (5): 1237-41 (1987)]**PEER REVIEWED**

Light and electron microscopic structure of lobar bronchial biopsies were examined of nine subjects with occupational asthma induced by **toluene** diisocyanate and of four control nonasthmatic subjects who had never been exposed to **toluene** diisocyanate. Inflammatory cell numbers were separately assessed in the intact epithelium, in the more superficial layer of the submucosa, and in the total submucosa. Asthmatic subjects had an increased number of inflammatory cells in the airway mucosa compared with control subjects. Eosinophils were significantly increased in all compartments, CD45-positive cells were significantly increased in the epithelium and in the more superficial layer of the submucosa, and mast cells were significantly increased only in epithelium. By electron microscopy eosinophils and mast cells appeare degranulated only in asthmatic patients. In the areas of epithelium that appeared intact by light microscopy, electron microscopy showed that, although the intercellular spaces between columnar cells were similar in asthmatic and control groups, the intercellular spaces between basal cells were significantly wider in patients with asthma. Patients with **toluene** diisocyanate induced asthma also had a thicker subepithelial reticular layer, where immunohistochemistry showed the presence of collagen III. In conclusion, in patients with asthma induced by **toluene** diisocyanate, the airway mucosa shows pathologic features, such as inflammatory cell infiltrate and thickening of subepithelial collagen, similar to those described in atopic asthma.
[Saetta M et al; Am Rev Respir Dis 145 (1): 160-8 (1992)]**PEER REVIEWED**

Serum neutrophil chemotactic activity, which is associated with mast cell or basophil activation, was quantitated to determine if mast cell or basophil mediators are released during bronchoprovocation-inhalation challenge with subirritant levels of **toluene** diisocyanate. Four subjects with suspected **toluene** diisocyanate induced asthma and four mite-sensitive subjects with asthma who served as a comparison group were studied. neutrophil chemotactic activity was measured in a multiwell, microchemotaxis chamber. Blood samples were collected, and forced expiratory volume in 1 second measurements were performed before challenge and at regular intervals during the subsequent 24 hr. Three of four workers clinically sensitive to **toluene** diisocyanate reacted to a subirritant **toluene** diisocyanate exposure. There was no increase in neutrophil chemotactic activity during placebo challenges. neutrophil chemotactic activity increased in the three **toluene** diisocyanate sensitive workers during early and late asthmatic reactions in quantities proportional to the forced expiratory volume in 1 second decline. No increase in neutrophil chemotactic activity was found during **toluene** diisocyanate exposures in the **toluene** diisocyanate negative worker. Gel filtration analysis demonstrated the main neutrophil chemotactic activity fraction eluted with macromolecules of an estimated molecular weight greater than 440,000 daltons. This characteristic is compatible with neutrophil chemotactic factor of basophil or mast cell origin. The kinetics of neutrophil chemotactic activity release were similar in mite- and **toluene** diisocyanate induced asthmatic reactions. A high correlation ($r = 0.97$; $p = 0.0006$) was obtained between the percent decrease in forced expiratory volume in 1 second during early asthmatic reactions and percent increase in neutrophil chemotactic activity. These observations support the hypothesis that activation of mast cells or basophils is associated with **toluene** diisocyanate induced early and late asthmatic reaction.
[Sastre J et al; J Allergy Clin Immunol 85 (3): 567-72 (1990)]**PEER

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In order to determine whether treatment with ketotifen inhibits asthmatic reactions induced by **toluene** di-isocyanate, six sensitized subjects with previously demonstrated dual or late asthmatic reaction after inhalation challenge with **toluene** diisocyanate were studied. Ketotifen (1 mg bid, orally) or placebo was administered for 7 days to the examined subjects, according to a double-blind, cross-over, placebo controlled study design. When the subjects were treated with either ketotifen or placebo, forced expiratory volume in 1 second markedly decr after exposure to **toluene** diisocyanate. These results suggest that the anti-asthmatic agent ketotifen is not effective in **toluene** diisocyanate induced asthma and suggest that it should not be used in the prophylaxis of asthmatic reactions induced by **toluene** diisocyanate in sensitized subjects.
[Tossin L et al; Clin Exp Allergy 19 (2): 177-82 (1989)]**PEER REVIEWED**

The beta-adrenoceptors on intact peripheral blood lymphocytes were studied in 21 allergic asthmatics, 11 **toluene** diisocyanate asthmatics and 17 normal subjects with radioligand binding assay technique. The airway responsiveness to methacholine provocation test was determined. The results indicated that beta-adrenoceptor Bmax values in allergic and **toluene** diisocyanate asthmatics were reduced but the affinity between receptor and ligand was increased; there was a positive correlation between the values of Bmax and forced expiratory volume in 1 second%, V25/Pr in both asthmatic groups, a positive correlation between the values of Bmax and PC20 in allergic asthmatics. The beta-adrenoceptor responsiveness was remarkably reduced in allergic asthmatics.
[Yang ZF et al; Chin J Tuberc Respir Dis 12 (3): 143-146, 190-191. (1989)]**PEER REVIEWED**

Leukotriene B4 release from the lungs of sensitized subjects during asthmatic reactions induced by **toluene** diisocyanate was investigated. Three groups of **toluene** diisocyanate sensitized subjects were examined, one after no exposure to **toluene** diisocyanate, the second 8 hr after an exposure to **toluene** diisocyanate that caused an early asthmatic reaction, and the third 8 hr after an exposure to **toluene** diisocyanate that caused a late asthmatic reaction. Bronchoalveolar lavage fluid was analysed by reverse-phase HPLC and by specific radioimmunoassay. The mean concn of leukotriene B4 was higher (0.31 + or - 0.09 (standard error) ng/ml, range 0.15-0.51) in bronchoalveolar lavage fluid of sensitized subjects who developed a late asthmatic reaction than in bronchoalveolar lavage fluid of subjects who developed an early asthmatic reaction (0.05 + or - 0.04 ng/ml, range 0-0.224), and no leukotriene B4 was detectable in the control subjects. Bronchoalveolar lavage was also performed 8 hr after **toluene** diisocyanate exposure on four **toluene** diisocyanate sensitized late-dual reactors who were on steroid treatment. In this group of subjects no leukotriene B4 was detectable. These results suggest that leukotriene B4 may be involved in late asthmatic reactions induced by **toluene** diisocyanate.
[Zocca E et al; J Appl Physiol 68 (4): 576-80 (1990)]**PEER REVIEWED**

Interactions:

The effects of methacholine inhalation on airway responsiveness in **toluene** diisocyanate induced asthma were studied in six workers with a history of sensitivity to **toluene** diisocyanate. Symptoms among subjects included shortness of breath, wheezing, cough, and chest tightness at work, during the evening, or at night. A detailed cllnical and occupational history was taken for each subject, and lung function measurement and skin intradermal tests for common allergens were conducted. Airway responsiveness to

methacholine was assessed before subjects were exposed for 30 minutes to 0.02 part per million **toluene** diisocyanate in an exposure chamber. Eight hours after **toluene** diisocyanate inhalation, airway responsiveness to methacholine was again determined. Forced expiratory volume was the measure of airway responsiveness. Although methacholine challenge was within normal limits when performed before **toluene** diisocyanate inhalation, the challenge went into the asthmatic range after **toluene** diisocyanate inhalation. Airway responsiveness increased significantly 8 hours after **toluene** diisocyanate challenge in the subjects and was accompanied by a decrease in forced expiratory volume. The late asthmatic reaction began between 3 and 5 hours asthma can be induced by **toluene** diisocyanate in the absence of airway responsiveness.
[Mapp CE et al; Eur J Respir Dis 68: 89-95 (1986)]**PEER REVIEWED**

TOLUENE DIISOCYANATE

CASRN: 26471-62-5

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Metabolism/Metabolites:

A technique for detectingurinary amine metabolites in rats exposed to **toluene** diisocyanate was evaluated. Skin tissue of rats was exposed to 40% **toluene**-2,4-diisocyanate solution in di-n-butyl-ether liquid. Rats were exposed daily for 3 hr on 4 consecutive days. Urine was collected in metabolic cages for 18 hr after the last exposure. Chromatographic techniques were used for nitrogen selective detection of nonderivatized amines. An autolinear temperature programmer was employed to analyze derivatized amine. The identity of the amine was confirmed by gas chromatography/mass spectrometry. A linear correlation was found between **toluene**-2,4-diamine added to urine and peak height. Peak height and recovery from the non hydrolyzed and from the hydrolyzed urine was about 85 and 70%, respectively. No free **toluene**-2,4-diamine or free **toluene**-2,4-diisocyanate was detected in the urine of rats exposed to **toluene**-2,4-diamine in hydrolyzed urine was 1.5 micrograms per milliliter. Gas chromatography/mass spectrometry confirmed the identity of the amine. /This/ highly sensitive technique tested is easy to apply and is effective for trace assays of amines.
[Rosenberg C; J Chromatography 323 (2): 429-33 (1985)]**PEER REVIEWED**

Epithelial injury and inflammation are involved in airway hyperresponsiveness and asthma induced by **toluene** diisocyanate. In that isocyanates are insoluble and highly reactive compounds, bronchial epithelial cells may represent the most important target cells of their toxic effect. We hypothesized that damage to airway epithelium by **toluene** diisocyanate may result in the release of metabolites of arachidonic acid, which are known to promote inflammation and to alter epithelial cell function and airway smooth muscle responsiveness. To test this hypothesis we examined eicosanoid products in the culture media of bronchial epithelial cells exposed in vitro to 8 and 18 ppb **toluene** diisocyanate. Epithelial cells derived from human bronchi obtained at surgery were cultured to confluency on collagen-coated microporous membranes. Those cells, which expressed differentiated characteristics of epithelial cells (they showed keratin-containing filaments and had a cobblestone appearance), were alternatively exposed to **toluene** diisocyanate or air for 30 min in a specially designed in vitro chamber. The production of metabolites of arachidonic acid was assessed by measuring the release of immunoreactive products into the cell medium at the end of the exposure and during a 2 hr period after exposure. This method revealed a predominant isocyanate induced release of immunoreactive 15-hydroxyeicosatetraenoic acid. Release rate of this compound tended to be dose-related and was associated with cell damage as assessed by the release of lactate dehydrogenase in the medium.
[Mattoli S et al; J Cell Physiol 142 (2): 379-85 (1990)]**PEER REVIEWED**

It has been previously shown that tachykinin depletion or antagonism prevented the increase in airway responsiveness to inhaled acetylcholine caused by exposure to **toluene** diisocyanate in awake guinea pigs. To insure that the effects of tachykinins were not limited to the extrathoracic airways and were not dependent on effects of **toluene** diisocyanate on baseline airway caliber, airway responsiveness to acetylcholine inhaled through tracheostomy in anesthetized and ventilated guinea pigs that were exposed to **toluene** diisocyanate or air after treatment with the tachykinin antagonist spantide, the tachykinin metabolism inhibitor phosphoramidon, or the vehicles for each drug were determined. When these drugs

were administered before and during **toluene** diisocyanate exposure, spantide significantly inhibited the **toluene** diisocyanate induced increase in acetylcholine responsiveness and phosphoramidon significantly potentiated this effect, whereas neither drug altered acetylcholine responsiveness in air exposed animals. To determine whether tachykinins were exerting their effect primarily during **toluene** diisocyanate exposure or during the subsequent acetylcholine challenge, the effect of each drug on acetylcholine responsiveness was also examined when the drugs were given after **toluene** diisocyanate exposure. At that time, spantide did not inhibit **toluene** diisocyanate induced acetylcholine hyperresponsiveness and phosphoramidon did not potentiate it. Neither drug nor **toluene** diisocyanate increased pulmonary resistance measured through a tracheostomy in these anesthetized and ventilated animals. These results suggest that the **toluene** diisocyanate induced increase in acetylcholine responsiveness is mediated by release of tachykinins into the intrathoracic airways during exposure to **toluene** diisocyanate.
[Sheppard D, Scypinski L; Am Rev Respir Dis 138 (3): 547-51 (1988)]**PEER REVIEWED**

Five men were exposed to **toluene** diisocyanate atmospheres for 7.5 hr. The **toluene** diisocyanate atmospheres were generated by a gas-phase permeation method, and the exposures were performed in an 8 cu m stainless steel test chamber. The mean air concn of **toluene** diisocyanate was ca 40 ug/cu m, which corresponds to the TLV of Sweden. The inhaled doses of 2,4- and 2,6-**toluene** diisocyanate were ca 120 ug. **Toluene** diisocyanate in the test chamber air was determined by an HPLC method using the 9-(N-methylaminomethyl)-anthracene reagent and by a continuous monitoring filter-tape instrument. After hydrolysis of plasma and urine, the related amines, 2,4- and 2,6-toluenediamine 2,4-, and 2,6-TDA), were determined as pentafluoropropionic anhydride derivatives by capillary gas-chromatography using selected ion monitoring in the electron-impact mode. The urinary elimination of the toluenediamines showed a possible biphasic pattern, with rapid first phases for 2,4-toluenediamine (mean half-life for the concn in urine, 1.9 hr) and for 2,6-toluenediamine (mean half-life for the concn in urine, 1.6 hr). The cumulative amount of 2,4-toluenediamine excreted in urine within 28 hr ranged from 8% to 14% of the estimated dose of 2,4-**toluene** diisocyanate, and the cumulative amount of 2,6-toluenediamine in urine ranged from 14% to 18% of the 2,6-**toluene** diisocyanate dose. The average urinary level of 2,4-toluenediamine was 5 ug/l in the 6 to 8 hr sample (range 2.8-9.6 ug/l), and the corresponding value fo 2,6-toluenediamine was 8.6 ug/l (range, 5.6-16.6 ug/l). Biological monitoring of exposure to 2,4- and 2,6-**toluene** diisocyanate by analysis of 2,4- and 2,6-toluenediamine in urine is feasible.
[Skarping G et al; Int Arch Occup Environ Health 63 (2): 83-8 (1991)]**PEER REVIEWED**

TOLUENE DIISOCYANATE

CASRN: 26471-62-5

For other data, click on the Table of Contents

Mechanism of Action:

SERUM FROM 26 PERSONS SHOWN TO REACT TO PROVOCATIVE INHALATION CHALLENGE WITH LOW CONCN OF **TOLUENE** DIISOCYANATE WAS TESTED BY RADIOALLERGOSORBENT TEST (RAST) USING A P-TOLYL ISOCYANATE-HUMAN SERUM ALBUMIN (TMI-HSA) CONJUGATE. POSITIVE RESULTS WERE OBTAINED IN 15-19% OF **TOLUENE** DIISOCYANATE REACTORS, DEPENDING ON THE METHOD OF EVALUTION. **TOLUENE** DIISOCYANATE ASTHMA MAY BE A COMPLEX SYNDROME WITH SEVERAL TYPES OF REACTIONS POSSIBLE, INCLUDING AN IMMUNOGLOBULIN-E MECHANISM IN SOME INDIVIDUALS. THE THEORY THAT **TOLUENE** DIISOCYANATE ASTHMA IS BASED SOLELY ON AN IMMUNE MECHANISM IS NOT SUPPORTED. THE FINDINGS DO NOT DISAGREE WITH THE HYPOTHESIS THAT **TOLUENE** DIISOCYANATE REACTIVITY MAY BE MEDIATED BY A PHARMACOLOGIC MECHANISM.
[BUTCHER BT ET AL; J ALLERGY CLIN IMMUNOL 66 (3): 213 (1980)]**PEER REVIEWED**

To investigate the role of pharmacological mechanisms in **toluene** diisocyanate induced occupational asthma, the effects of **toluene** diisocyanate on rat trachea ring and lung parenchymal strip were studied in vitro. The most prominent effect observed was a stimulation of metacholine induced contraction of the tracheal ring by 1M **toluene** diisocyanate (added in dimethyl sulfoxide). The results were less pronounced when **toluene** diisocyanate was added from a stock solution prepared in water, which is possibly due to copolymerisation. It is concluded that the pharmacological effect of **toluene** diisocyanate may result from an autonomic imbalance between cholinergic and B-adrenergic neural control.
[Borm PJA et al; Br J Ind Med 46 (1): 56-9 (1989)]**PEER REVIEWED**

A study of the occurrence of serum immunoglobulin-E and immunoglobulin-G antibodies in workers with isocyanate induced asthma was conducted. The study group consisted of 62 workers (58 males) being evaluated for occupational asthma. Thirty nine had been exposed to hexamethylene diisocyanate, 17 to diphenylmethane diisocyanate, and six to **toluene** diisocyanate. The subjects completed a respiratory and occupational questionnaire. Spirometric tests were administered. Skin prick tests were performed with 15 common inhalant allergens and **toluene** diisocyanate, hexamethylene diisocyanate, and diphenylmethane diisocyanate human serum albumin conjugates. Blood samples were collected and assayed for specific serum immunoglobulin-G and immunoglobulin-E antibodies to hexamethylene diisocyanate, diphenylmethan diisocyanate, and **toluene** diisocyanate. Specific inhalation challenges were conducted with hexamethylene diisocyanate, diphenylmethane diisocyanate, and **toluene** diisocyanate. Specific inhalation challenge with **toluene** diisocyanate, hexamethylene diisocyanate, or diphenylmethane diisocyanate induced significant bronchoconstriction in half of the subjects, late reactions being the most common. Twenty subjects had significantly elevated immunoglobulin-G concn and nine had significantly elevated immunoglobulin-G plus immunoglobulin-E concn. Six of 12 subjects with elevated immunoglobulin-E and immunoglobulin-G antibodies had positive skin prick tests for hexamethylene diisocyanate and one was sensitized to diphenylmethane diisocyanate. It was concluded that an association between isocyanate specific antibodies and the results of specific inhalation challenge tests has been established. This suggests that isocyanate induced asthma may involve an immunological

mechanism.
[Cartier A et al; J Allergy Clin Immunol 84 (4 Part 1): 507-14 (1989)]**PEER REVIEWED**

The influence of cyclophosphamide induced granulocyte depletion on **toluene** diisocyanate related changes in airway reactivity and pathology was assessed in guinea pigs. Twelve cyclophosphamide-treated and 12 control animals comprising each group were studied physiologically before and 2 hr after a single 10 min exposure to 3 ppm of **toluene** diisocyanate. Reactivity was determined in intact unanesthetized animals by measuring specific airway conductance before and during intravenous acetylcholine infusion. After testing, tracheal tissue for light microscopic examination was obtained from three hyperreactive guinea pigs in each exposed group and compared with tissue from treated and control animals (n = 3 each) that had not been **toluene** diisocyanate exposed. Cyclophosphamide treatment caused substantial decr in both circulating and airway granulocyte counts. However, the incidence and degree of bronchial hyperreactivity that occurred 2 hr post-**toluene** diisocyanate was similar in the untreated and treated groups. Results indicate that **toluene** diisocyanate induced bronchial hyperreactivity 1) occurs shortly after a brief high concn exposure and 2) appears independent of circulating or airway granulocyte counts.
[Cibulas W Jr et al; J Appl Physiol 64 (5): 1773-8 (1988)]**PEER REVIEWED**

To determine the importance of airway inflammation for the development of late asthmatic reactions, we examined sensitized subjects during late asthmatic reactions induced by exposure to **toluene** diisocyanate in the laboratory. Late asthmatic reactions are associated with a transient increase of bronchial responsiveness and, at the same time, with an increase of neutrophils followed by eosinophils, and of leukotriene B4 and albumin in bronchoalveolar lavage fluid. Late asthmatic reactions, increased bronchial responsiveness, and increase of neutrophils, eosinophils, leukotriene B4, and albumin concn in bronchoalveolar lavage induced by exposure to **toluene** diisocyanate are all prevented by pretreatment with prednisone but not with the nonsteroidal anti-inflammatory agent indomethacin. Aerosolized steroids (beclomethasone and dexamethasone isonicotinate) completely inhibit late asthmatic reactions induced by **toluene** diisocyanate, whereas theophylline has a partial, and verapamil, ketotifen, and cromolyn have no protective effect. These results suggest that late asthmatic reactions induced by **toluene** diisocyanate may be caused by airway inflammation, and that anti-inflammatory steroids should be recommended in the prophylaxis of **toluene** diisocyanate asthma.
[Fabbri LM et al; Am Rev Respir Dis 143 (3 Pt 2): 537-8 (1991)]**PEER REVIEWED**

The effects of **toluene** diisocyanate on T-cell subpopulations and circulating lymphocytes in ten persons (five males)): 19 to 50 yr old, with **toluene** diisocyanate induced occupational asthma were examined. Five subjects revealed early and late asthmatic reactions to **toluene** diisocyanate (dual responders) and five revealed late asthmatic reactions (late responders). Subjects underwent inhalation challenge with 0.005 to 0.015 ppm **toluene** diisocyanate or filtered air for 10 to 30 min on two occasions. One second forced expiratory volumes were measured before and at periodic intervals between 30 min and 24 hr after challenge. Venous blood samples were drawn 30 min and 8, 24, 48, and 72 hr after **toluene** diisocyanate. Total and differential leukocyte counts and T-cell subpopulations were determined. The five dual responders demonstrated forced expiratory volume in 1 sec decreased indicative of early and late asthmatic reactions and the five late responders demonstrated forced expiratory volume in 1 second decr indicative of a late asthmatic reaction. **Toluene** diisocyanate challenge did not affect the number of

circulating erythrocytes and leukocytes. The percentage of eosinophils was significantly increased 24 hr after challenge and sustained for up to 48 hr. The percentages of neutrophils, lymphocytes, and monocytes were not altered by **toluene** diisocyanate. Among the T-lymphocyte subpopulation, the proportion of CD8(+) lymphocytes was significantly increased 8 hr after **toluene** diisocyanate challenge. The increase was more pronounced in the lat responders. An additional increase in CD8(+) lymphocytes occurred 48 hr post exposure in seven subjects but was unrelated to responder type. The number of CD4(+) cells did not change. This resulted in a decrease in the CD4(+)/CD8(+) ratio 8 and 48 hr after **toluene** diisocyanate challenge. It was concluded that **toluene** diisocyanate induced late asthmatic reactions are associated with an increase in the number of suppressor/cytotoxic lymphocytes and eosinophils in peripheral blood.
[Finotto S et al; Br J Ind Med 48 (2):116-21 (1991)]**PEER REVIEWED**

Intravenously administered endotoxin inhibits the polymorphonuclear leukocyte dependent airway edema produced in guinea pigs exposed to **toluene** diisocyanate. Tumor necrosis factor is produced in vivo by peripheral blood monocytes and tissue macrophages stimulated with endotoxin and has been shown to activate polymorphonuclear leukocyte's and vascular endothelial cells. To determine whether the inhibition of airway edema is mediated by tumor necrosis factor, guinea pigs were treated with intravenous saline or 75,000 U/kg recombinant human tumor necrosis factor 1.5 hr before exposure to air or 3 ppm **toluene** diisocyanate for 1 hr. Animals were then injected intravenously with 50 mg/kg Evans blue dye as a marker of protein extravasation. Saline-treated animals exposed to **toluene** diisocyanate had a significant increase in tracheal Evans blue dye extravasation (85 + or - 6.5 ug dye/g trachea, mean + or - standard error) compared with saline-treated animals exposed to air (31.3 + or - 2.5, $P < 0.001$). The tracheal extravasation of Evans blue dye was significantly inhibited ($P < 0.05$) in **toluene** diisocyanate exposed animals treated with tumor necrosis factor (64.7 + or - 7.5). Neither heat-inactivated tumor necrosis factor (104.9 + or - 9.5) nor tumor necrosis factor neutralized with a monoclonal antibody against tumor necrosis factor (99.7 + or - 17.9) inhibited **toluene** diisocyanate induced airway edema. In addition, treatment with 15,000 U/kg (99.9 + or - 21.3) or 150,000 U/kg (103.2 + or - 17.6) interleukin 1, a monokine also produced in response to endotoxin, did not prevent airway edema. These results suggest that tumor necrosis factor released in response to endotoxin mediates endotoxin's inhibition of a polymorphonuclear leukocyte dependent airway edema.
[Gordon T, Sheppard D; J Appl Physiol 64 (4): 1988 1688-92]**PEER REVIEWED**

Serum immunoglobulin-G and immunoglobulin-E to isocyanate haptenized human serum albumin (HSA) were estimated by ELISA in 55 isocyanate workers who underwent isocyanate inhalation challenge studies in Montreal, Canada. The challenges were negative in 29 workers and positive in 26 workers. Isocyanate antibodies were estimated by ELISA index. The mean immunoglobulin-G indices were found to be significantly higher in the challenge-positive workers, and there was a similar trend for the immunoglobulin-E indices. Antibody specificities for **toluene** diisocyanate-human serum albumin, diphenylmethane diisocyanate-human serum albumin, and hexamethylene diisocyanate-human serum albumin were determined by inhibition studies with a variety of isocyanate haptenized carriers. The other isocyanate substituted carriers were either noninhibitory or caused only partial inhibition as contrasted with the complete inhibition achieved by human serum albumin conjugated to the isocyanate to which the worker was exposed. We interpret these specificity studies as indicating that the inhalation of isocyanates results in production of antibody that recognizes new antigenic determinants that develop from the coupling of isocyanates to homologous proteins.

[Grammer LC et al; J Allergy Clin Immunol 86 (1): 94-8 (1990)]**PEER REVIEWED**

Inhalation of **toluene** diisocyanate results in toxic responses ranging from pulmonary irritation to immunological sensitization. The use of radioactively labeled isocyanate has made it possible to follow the initial uptake of the compound into the bloodstream independent of the final fate of the isocyanate. This study shows that the rate of uptake into the blood is linear during exposure to concn ranging from 0.00005 to 0.146 ppm and that the uptake continues to increase slightly postexposure. It also demonstrates that the radioactivity clears from the bloodstream to a level corresponding to approximately a 100 nM concn of tolyl group after 72 hr and persists at a nanomolar level even 2 wk following the exposure. The initial rate of (14)C uptake is also a linear function of the concn of **toluene** diisocyanate when expressed either as concn (ppm) or as concn multiplied by duration of exposure (ppm.hr). This is discussed in comparison with the toxic responses as a function of both ppm and ppm.hr. Finally, the inclusion of the data on methyl isocyanate indicates that the uptake into arterial blood is a function of exposure concn, independent of isocyanate structure.
[Kennedy AL et al; Toxicol Appl Pharmacol 100 (2): 280-92 (1989)]**PEER REVIEWED**

Isocyanates are an important cause of occupational asthma. The mechanism of isocyanate induced asthma is still unknown. To determine whether **toluene** diisocyanate stimulates the 'efferent' function of peripheral endings of capsaicin-sensitive sensory nerves, we investigated the effect of **toluene** diisocyanate in the rat isolated urinary bladder, a preparation in which the action of capsaicin has been well characterized. **Toluene** diisocyanate (0.03 mM) produced a concn dependent contraction of the bladder strips. It maximal effect was about 50 % of the response to capsaicin (1 uM). Previous exposure of the strips to capsaicin followed by washing out produced complete unresponsiveness, both to the first exposure to **toluene** diisocyanate and to a second exposure of capsaicin. Further, the response to both **toluene** diisocyanate and capsaicin was completely prevented by extrinsic bladder denervation, achieved by bilateral removal of pelvic ganglia (72 hr before). Repeated exposure of the rat bladder to **toluene** diisocyanate reduced the capsaicin-evoked release of calcitonin gene-related peptide like immunoreactivity (CGRP-LI), taken as biochemical marker of activation of these sensory nerves. These experiments provide the first evidence that **toluene** diisocyanate activates directly or indirectly the efferent function of capsaicin-sensitive primary sensory nerves.
[Mapp CE et al; Eur J Pharmacol 180 (1): 113-8 (1990)]**PEER REVIEWED**

The in vivo exposure to an asthmogenic stimulus, **toluene** diisocyanate, causes airway epithelial damage associated with inflammation and increased bronchial hyperresponsiveness. The latter mechanisms might partly be mediated by the release of eicosanoids from bronchial epithelial cells. Previously it has been demonstrated that the in vitro exposure of bronchial epithelial cells to **toluene** diisocyanate results in the release of immunoreactive 15-hydroxyeicosatetraenoic acid, a product of activation of the 15-lipoxygenase pathway with inflammatory properties. Present study shows that **toluene** diisocyanate induced release of 15-hydroxyeicosatetraenoic acid from epithelial cells can be prevented by nedocromil sodium, an anti-asthmatic drug with anti-inflammatory properties. This mode of action of the compound may explain its clinical effectiveness in asthma.
[Mattoli S et al; Int Arch Allergy Appl Immunol 92 (1): 16-22 (1990)]**PEER REVIEWED**

To determine whether early and/or late asthmatic responses induced by **toluene** diisocyanate are caused by a reflex mechanism involving stimulation of muscarinic receptors, we studied the effect of the muscarinic antagonist atropine on early and late airway response induced by **toluene** diisocyanate. A preliminary study was conducted in asthmatics to assess whether the selected dose of atropine provided adequate muscarinic blockade. On different days we measured the provocation dose (in mg) of carbachol causing a 15% decrease in forced expiratory volume in 1 second (PD15FEV1) without and with atropine premedication (0.008 or 0.012 mg/kg sc atropine 30 or 90 min before carbachol challenge test). 0.008 to 0.012 mg/kg sc atropine increased the PD15FEV1 carbachol by 6 to 10 fold, inducing a consistent and prolonged decrease in nonspecific bronchial hyperresponsiveness to cholinergic agent. 10 Subjects with a history of sensitization to **toluene** diisocyanate were then examined in 2 sets of experiments. In the first set of experiments, the subjects were studied before and after exposure to **toluene** diisocyanate (0.04 ppm; 30 min) after no treatment. In the second set of experiments, carried out 1 to 2 wk later, the same procedure was repeated after treatment with atropine (0.008 to 0.012 mg/kg atropine sulfate administered sc 30 min before **toluene** diisocyanate challenge, and then at 90 min intervals after **toluene** diisocyanate exposure); all patients showed symptoms of atropine effect (dryness of mouth, cycloplegia, increased heart rate).
[Paggiaro P et al; Am Rev Respir Dis 136 (5): 1237-41 (1987)]**PEER REVIEWED**

Light and electron microscopic structure of lobar bronchial biopsies were examined of nine subjects with occupational asthma induced by **toluene** diisocyanate and of four control nonasthmatic subjects who had never been exposed to **toluene** diisocyanate. Inflammatory cell numbers were separately assessed in the intact epithelium, in the more superficial layer of the submucosa, and in the total submucosa. Asthmatic subjects had an increased number of inflammatory cells in the airway mucosa compared with control subjects. Eosinophils were significantly increased in all compartments, CD45-positive cells were significantly increased in the epithelium and in the more superficial layer of the submucosa, and mast cells were significantly increased only in epithelium. By electron microscopy eosinophils and mast cells appeare degranulated only in asthmatic patients. In the areas of epithelium that appeared intact by light microscopy, electron microscopy showed that, although the intercellular spaces between columnar cells were similar in asthmatic and control groups, the intercellular spaces between basal cells were significantly wider in patients with asthma. Patients with **toluene** diisocyanate induced asthma also had a thicker subepithelial reticular layer, where immunohistochemistry showed the presence of collagen III. In conclusion, in patients with asthma induced by **toluene** diisocyanate, the airway mucosa shows pathologic features, such as inflammatory cell infiltrate and thickening of subepithelial collagen, similar to those described in atopic asthma.
[Saetta M et al; Am Rev Respir Dis 145 (1): 160-8 (1992)]**PEER REVIEWED**

Serum neutrophil chemotactic activity, which is associated with mast cell or basophil activation, was quantitated to determine if mast cell or basophil mediators are released during bronchoprovocation-inhalation challenge with subirritant levels of **toluene** diisocyanate. Four subjects with suspected **toluene** diisocyanate induced asthma and four mite-sensitive subjects with asthma who served as a comparison group were studied. neutrophil chemotactic activity was measured in a multiwell, microchemotaxis chamber. Blood samples were collected, and forced expiratory volume in 1 second measurements were performed before challenge and at regular intervals during the subsequent 24 hr. Three of four workers clinically sensitive to **toluene** diisocyanate reacted to a subirritant **toluene**

diisocyanate exposure. There was no increase in neutrophil chemotactic activity during placebo challenges. neutrophil chemotactic activity increased in the three **toluene** diisocyanate sensitive workers during early and late asthmatic reactions in quantities proportional to the forced expiratory volume in 1 second decline. No increase in neutrophil chemotactic activity was found during **toluene** diisocyanate exposures in the **toluene** diisocyanate negative worker. Gel filtration analysis demonstrated the main neutrophil chemotactic activity fraction eluted with macromolecules of an estimated molecular weight greater than 440,000 daltons. This characteristic is compatible with neutrophil chemotactic factor of basophil or mast cell origin. The kinetics of neutrophil chemotactic activity release were similar in mite- and **toluene** diisocyanate induced asthmatic reactions. A high correlation (r = 0.97; p = 0.0006) was obtained between the percent decrease in forced expiratory volume in 1 second during early asthmatic reactions and percent increase in neutrophil chemotactic activity. These observations support the hypothesis that activation of mast cells or basophils is associated with **toluene** diisocyanate induced early and late asthmatic reaction.
[Sastre J et al; J Allergy Clin Immunol 85 (3): 567-72 (1990)]**PEER REVIEWED**

In order to determine whether treatment with ketotifen inhibits asthmatic reactions induced by **toluene** di-isocyanate, six sensitized subjects with previously demonstrated dual or late asthmatic reaction after inhalation challenge with **toluene** diisocyanate were studied. Ketotifen (1 mg bid, orally) or placebo was administered for 7 days to the examined subjects, according to a double-blind, cross-over, placebo controlled study design. When the subjects were treated with either ketotifen or placebo, forced expiratory volume in 1 second markedly decr after exposure to **toluene** diisocyanate. These results suggest that the anti-asthmatic agent ketotifen is not effective in **toluene** diisocyanate induced asthma and suggest that it should not be used in the prophylaxis of asthmatic reactions induced by **toluene** diisocyanate in sensitized subjects.
[Tossin L et al; Clin Exp Allergy 19 (2): 177-82 (1989)]**PEER REVIEWED**

The beta-adrenoceptors on intact peripheral blood lymphocytes were studied in 21 allergic asthmatics, 11 **toluene** diisocyanate asthmatics and 17 normal subjects with radioligand binding assay technique. The airway responsiveness to methacholine provocation test was determined. The results indicated that beta-adrenoceptor Bmax values in allergic and **toluene** diisocyanate asthmatics were reduced but the affinity between receptor and ligand was increased; there was a positive correlation between the values of Bmax and forced expiratory volume in 1 second%, V25/Pr in both asthmatic groups, a positive correlation between the values of Bmax and PC20 in allergic asthmatics. The beta-adrenoceptor responsiveness was remarkably reduced in allergic asthmatics.
[Yang ZF et al; Chin J Tuberc Respir Dis 12 (3): 143-146, 190-191. (1989)]**PEER REVIEWED**

Leukotriene B4 release from the lungs of sensitized subjects during asthmatic reactions induced by **toluene** diisocyanate was investigated. Three groups of **toluene** diisocyanate sensitized subjects were examined, one after no exposure to **toluene** diisocyanate, the second 8 hr after an exposure to **toluene** diisocyanate that caused an early asthmatic reaction, and the third 8 hr after an exposure to **toluene** diisocyanate that caused a late asthmatic reaction. Bronchoalveolar lavage fluid was analysed by reverse-phase HPLC and by specific radioimmunoassay. The mean concn of leukotriene B4 was higher (0.31 + or - 0.09 (standard error) ng/ml, range 0.15-0.51) in bronchoalveolar lavage fluid of sensitized subjects who developed a late asthmatic reaction than in bronchoalveolar lavage fluid of subjects who

developed an early asthmatic reaction (0.05 + or - 0.04 ng/ml, range 0-0.224), and no leukotriene B4 was detectable in the control subjects. Bronchoalveolar lavage was also performed 8 hr after **toluene** diisocyanate exposure on four **toluene** diisocyanate sensitized late-dual reactors who were on steroid treatment. In this group of subjects no leukotriene B4 was detectable. These results suggest that leukotriene B4 may be involved in late asthmatic reactions induced by **toluene** diisocyanate.
[Zocca E et al; J Appl Physiol 68 (4): 576-80 (1990)]**PEER REVIEWED**

TOLUENE DIISOCYANATE

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Pharmacology:

Interactions:

The effects of methacholine inhalation on airway responsiveness in **toluene** diisocyanate induced asthma were studied in six workers with a history of sensitivity to **toluene** diisocyanate. Symptoms among subjects included shortness of breath, wheezing, cough, and chest tightness at work, during the evening, or at night. A detailed cllnical and occupational history was taken for each subject, and lung function measurement and skin intradermal tests for common allergens were conducted. Airway responsiveness to methacholine was assessed before subjects were exposed for 30 minutes to 0.02 part per million **toluene** diisocyanate in an exposure chamber. Eight hours after **toluene** diisocyanate inhalation, airway responsiveness to methacholine was again determined. Forced expiratory volume was the measure of airway responsiveness. Although methacholine challenge was within normal limits when performed before **toluene** diisocyanate inhalation, the challenge went into the asthmatic range after **toluene** diisocyanate inhalation. Airway responsiveness increased significantly 8 hours after **toluene** diisocyanate challenge in the subjects and was accompanied by a decrease in forced expiratory volume. The late asthmatic reaction began between 3 and 5 hours asthma can be induced by **toluene** diisocyanate in the absence of airway responsiveness.
[Mapp CE et al; Eur J Respir Dis 68: 89-95 (1986)]**PEER REVIEWED**

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Environmental Fate & Exposure:

Environmental Fate/Exposure Summary:

Commercial **toluene** diisocyanate (TDI) is composed of 2 isomers. 2,4-**Toluene** diisocyanate constitutes roughly 80% of TDI, the other 20% being the 2,6-isomer. It may be released to the environment as fugitive emissions and from stack exhaust during the production, transport, and use of TDI in the manufacture of polyurethane foam products and coatings as well as from spills. The types of reactions which the isomers undergo are similar, although the rates may differ. The reactivity of the 2,4-**toluene** diisocyanate with active hydrogen is greater than with the 2,6-isomer, therefore the percentage of 2,4-**toluene** diisocyanate in monitored TDI is generally much less than the 80% in the commercial mixture. However, since much of the monitoring data do not distinguish between isomers, it is not possible to know the proportion of the isomers in the TDI. If spilled on wet land, TDI is rapidly degraded. In one experiment simulating a spill, 5.5% of the original material remained after 24 hours and in a field situation, the concentration of TDI had declined to the ppm levels in 12 weeks. If released into water, a crust forms around the liquid TDI and <0.5% of the original material remains after 35 days. Low concentrations of TDI disappear from the aqueous environment in approximately a day. In the atmosphere, TDI reacts with photochemically produced hydroxyl radicals (half-life 3.3 hr) and is also removed by dry deposition. Human exposure is primarily occupational via inhalation and dermal contact. (SRC)

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Probable Routes of Human Exposure:

Exposure to **toluene** diisocyanate is primarily occupational via inhalation or dermal contact with the aerosol or vapor. Workers may also be exposed through skin contact with freshly cured foam or as a result of spills or splashes. (SRC)

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THE RESPIRATORY HEALTH OF 277 WORKERS IN A NEW **TOLUENE** DIISOCYANATE (TDI) MANUFACTURING PLANT WAS STUDIED PROSPECTIVELY DURING 5 YR OF EXPOSURE. PERSONAL TDI MONITORS WERE USED TO CONTINUOUSLY MEASURE PEAK & 8-HR TIME-WEIGHTED AVG (TWA) CONCN IN MORE THAN 2000 SAMPLES. REGRESSION OF ANNUAL CHANGE ON SMOKING (PACK-YEARS), ATOPIC STATUS & CUMULATIVE TDI EXPOSURE, DICHOTOMIZED AT 68.2 PPB MONTHS INTO LOW & HIGH EXPOSURE GROUPS, SHOWED SIGNIFICANT EFFECTS OF SMOKING ON SPIROMETRIC TESTS & LUNG VOLUMES. AFTER ADJUSTING FOR PACK-YEARS OF SMOKING, THE 74 MEN IN THE HIGH CUMULATIVE TDI EXPOSURE CATEGORY HAD SIGNIFICANTLY LARGER DECLINE IN FEV1 (1-S FORCED EXPIRATORY VOLUME), % FEV (% FORCED EXPIRATORY VOLUME) & FEF25-75% (FORCED EXPIRATORY FRACTION FROM 25 TO 75% VITAL CAPACITY) THAN DID THE 149 MEN IN THE LOW CATEGORY. ANNUAL CHANGE IN FEV1 WAS THEN EXAMINED IN 6 SMOKING-EXPOSURE CATEGORIES: IN NEVER-SMOKERS, AVG ANNUAL DECLINE WAS 38 ML/YR GREATER IN THOSE WITH HIGHER CUMULATIVE TDI

EXPOSURE.
[DIEM JE ET AL; AM REV RESPIR DIS 126 (3): 420 (1982)]**PEER REVIEWED**

VAPORS OF THESE COMPD INVARIABLY BECOME AIRBORNE IN POLYMERIZATION REACTIONS, ESP SINCE HEAT & GAS ARE EVOLVED. /**TOLUENE** DIISOCYANATES/
[Hamilton, A., and H. L. Hardy. Industrial Toxicology. 3rd ed. Acton, Mass.: Publishing Sciences Group, Inc., 1974. 335]**PEER REVIEWED**

NIOSH (NOHS Survey 1972-1974) has statistically estimated that 29,284 workers are exposed to TDI in the USA(1). NIOSH (NOES Survey 1981-1983) has statistically estimated that 6,044 workers are exposed to TDI in the USA(2). Since the NOES survey excludes exposure to trade name chemicals which may contain the chemical, occupational exposure could be considerably higher(SRC).
[(1) NIOSH; National Occupational Health Survey (1974) (2) NIOSH; National Occupational Exposure Survey (1983)]**PEER REVIEWED**

Concentration medians for 2,4-**toluene** diisocyanate in 2 plants producing flexible polyurethane foam were 0.70 and 0.33 ppb for the mixing and finishing ends, respectively(1). The respective median values for 2,6-TDI were 0.91 and 1.1 ppb. Maximum concentrations of 2,6-TDI exceeded 64 ppb at the finishing end(1).
[(1) Rando RJ et al; Am Ind Hyg Assoc J 45: 199-203 (1984)]**PEER REVIEWED**

In a Finnish study, TDI vapor concentrations ranged from 25-80 ug/cu m for pouring, 14-44 ug/cu m for paper stripping, and 1-8 ug/cu m for cutting(1). Personal monitors measured 9-34 ug/cu m and 5-30 ug/cu m of the 2,4-isomer for pouring and paper stripping, respectively(1). While 2,4-**toluene** diisocyanate constitutes 80% of TDI, and 2,6-**toluene** diisocyanate 20%, the 2,4-isomer is more reactive so that the concentration of the 2,6-isomer is higher in workplace air(1). The percentage of 2,4-**toluene** diisocyanate to total **toluene** diisocyanate measured with the personal monitors ranged from 29 to 69%(1). TDI levels of 1.3-2.8 ppb were detected in air inside a Swedish factory manufacturing polyurethanes(2).
[(1) Rosenberg C, Savolainen H; J Chromatography 367: 385-92 (1986) (2) Audunsson G et al; Intern J Environ Anal Chem 20: 85-100 (1985)]**PEER REVIEWED**

Mean concn ranges of TDI reported in ambient workplace air were 0.7-710 ug/cu m in TDI production, ND - 1490 ug/cu m during polyurethane foam production, 70-140 mg/cu m during elastomer production, 13 - 1050 ug/cu m during polyurethane foam use, 10-710 ug/cu m during polyurethane spray paint use, and <1-740 ug/cu m during the production of polyurethane-coated wire(1). Mean concn in personal samples ranged from ND-540 ug/cu m during polyurethane foam production and 2-1220 ug/cu m during polyurethane spray foam use(1). Additionally, mean concn of TDI released from insulation in a ship's hold was reported to be 120-150 ug/cu m and that released from coated fabric in a workplace 2-10 ug/cu m(1). During the outdoor application of TDI foam to a 40 ft diameter storage tanks, the mean atmospheric TDI concentration downwind from the spray gun was 0.3 ppm at 8 ft, 0.02 ppm at 40 ft, and 0.002 ppm at 150 ft(2). TDI was not detected more than 8 ft upwind of the spray gun(2). Air samples taken within two ft of the foam surface immediately after spraying had ceased was found to be 0.03 ppm(2). Mean TDI concentrations near the pumping equipment during material transfer was 0.02

ppm(2).
[(1) IARC Monograph on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. 39: 287-323 (1985) (2) Peterson JE et al; Amer Id Hyg Assoc J 23: 345-52 (1962)]**PEER REVIEWED**

Natural Pollution Sources:

2,4- and 2,6-**toluene** diisocyanate, the components of commercial TDI are not known to occur as a natural product(1).
[(1) IARC; Monograph on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. 19: 303-11 (1979)]**PEER REVIEWED**

Artificial Pollution Sources:

Levels of 100-17,700 ug/cu m **toluene** diisocyanate were reported in samples from the stack exhaust of a polyurethane foam production plant.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 299 (1986)]**PEER REVIEWED**

TDI may be released to the environment, primarily as stack and fugitive emissions into air during its commercial production, handling, and processing prior to polyurethane foam production(1). It may also be released during the manufacture of polyurethane foam products and coatings, from sprays, insulation materials, and polyurethane foam coated fabrics(1,3). About 0.005% of the TDI used in flexible foam slabstock plants is released in vent stack exhaust and this contains <50% of the 2,4-isomer(2). Large quantities of TDI are transported by rail, road, and sea and releases may occur from accidental spills on land or in surface waters during loading or transit(2).
[(1) IARC Monograph on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. 39: 287-323 (1985) (2) Brochhagen FK, Grieveson BM; Cellular Polymers 3: 11-7 (1984) (3) Duff PB; pp. 408-12 in Polyurethane-New Paths to Progress Marketing Technology Proc of the SPI 6th Inter Tech/Market Conf (1983)]**PEER REVIEWED**

Environmental Fate:

TERRESTRIAL FATE: Ten days after a spill of 13 tons of **toluene** diisocyanate (TDI) onto swampy, wet forest soil, TDI and toluenediamines were found in the soil(1,2). The TDI solidified and the area was covered with sand. The soil concn of TDI and toluenediamine combined declined from the parts per thousand to parts per million range between 10 days and 12 wk after the spill(2). No TDI was detected in a connecting brook 10 days after the spill(2). After 6 years only TDI-derived polyureas were found at the site(1). In a simulated spill, 5 kg of TDI in a container was covered with 50 kg of sand and 5 kg of water at ambient temperatures and samples taken from the top and bottom of the sand pile. After 24 hr, 5.5% of the TDI remained unreacted and after 8 days 3.5% remained(2). The reaction product was largely polyureas(2).
[(1) IARC Monograph on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. 39: 287-323 (1985) (2) Brochhagen FK, Grieveson BM; Cellular Ploymers 3: 11-7 (1984)]**PEER REVIEWED**

AQUATIC FATE: When low concns of TDI are released into model river or seaway systems, it is hydrolyzed within a day. In order to simulate a spill of TDI in stagnant water, 0.5 liters of TDI was poured into 20 liters of water of pH 5, 7, or 9 at 20 deg C. A hard compact crust formed at the water TDI interface(1). This crust thickened over a period of 30 days until no liquid TDI remained. The solid crust contained <0.5% of the original TDI after 35 days(1). Another experiment were performed to simulate a spill into running water by pouring 0.5 l of TDI into 20 l of slowly overflowing water. Barely detectable amounts of toluenediamine were present in the overflow samples. As in the stagant water simulation, a crust formed that contained <0.5% of the original TDI after 35 days(1).
[(1) Brochhagen FK, Grieveson BM; Cellular Ploymers 3: 11-17 (1984)]**PEER REVIEWED**

ATMOSPHERIC FATE: Removal of TDI from the atmosphere is due to reaction with photochemically produced hydroxyl radicals (half-life 3.3 hr) as well as through dry deposition. Earlier ideas that reaction with water vapor was of major importance have not been substantiated in recent experiments.(SRC)
PEER REVIEWED

Environmental Biodegradation:

Toluene diisocyanates are expected to be hydrolyzed much more rapidly than they are attacked by microorganisms. The resulting **toluene** diamines are subject to a wide variety of biochemical transformations.
[ITC/USEPA; Information Review #231 (Draft) Toluene Diisocyanates p. 19 (1981)]**PEER REVIEWED**

Environmental Abiotic Degradation:

Toluene diisocyanate reacts readily with compounds containing active hydrogens, such as water, acids, and alcohols(2). Contact with bases may cause uncontrollable polymerization with rapid evolution of heat(2). In concentrated solutions, hydrolysis of one of the isocyanate groups to the amine is followed by rapid reaction of the amine with an isocyanate group on another molecule leading to dimers, oligimers, and polymers(2). In one experiment the hydrolysis product yield was 20% diamine and 80% polyurea(3). When 50 ppm of **toluene** diisocyanate was added to model river and seawater systems, the concn fell to 0.1 ppm or less at the end of 1 day(1).
[(1) Duff PB; The Fate of TDI in the Environment. In: Polyurethane-New Paths to Progress Marketing Technology. Proc. of the SPI 6th Inter. Tech. Marketing Conf. pp. 408-12 (1983) (2) IARC Monograph on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. 39: 287-323 (1985) (3) Sopach ED, Boltromeyuk LP; Gig Sanit 7: 10-3 (1974)]**PEER REVIEWED**

Gas phase loss of TDI was originally thought to be due to reaction of TDI with water vapor. One early work showed that the percent disappearance of TDI in air depended almost solely on the water vapor concentration, increasing 3.2% per unit increase in absolute humidity (g water/kg dry air), so that at 15 g water/kg dry air, a 50% reduction in TDI was obtained(2). These reductions were obtained after 8 sec and did not differ appreciably after 75 sec(2). More recent work contradicted these earlier findings and a program was instituted to study the gas-phase reactions between TDI and water using a room sized environmental chamber(1). They found that over a relative humidity range of 7-70%, the loss rate of TDI was independent of humidity and no toluenediamine or TDI-urea products could be detected(1). No

evidence of gas phase reaction between water and TDI could be detected. The loss of TDI was due to adsorption to the chamber walls(1).
[(1) Holdren MW et al; Am Ind Hyg Assoc J 45: 626-33 (1984) (2) Dyson WL, Hermann ER; Amer Ind Hyg Assoc J 32: 741-4 (1971)]**PEER REVIEWED**

Subsequent experiments were performed in the environmental chamber to assess the importance of photolysis, reaction with free radicals, and adsorption onto particulate matter as atmospheric removal processes(1). The loss rate of TDI in irradiated clean air was first order with a half-life of 3.3 hr(1). By using a free radical scavenger, it was shown that free-radicals and not photolysis was responsible for the removal. The half-life is consistant with the reaction with photochemically generated hydroxyl radicals(1). The addition of a urban surrogate hydrocarbon mixture (polluted urban air), did not significantly alter removal rates(1). The concentration of hydroxyl radicals generally increases in polluted air resulting in shorter half-lives which were not observed in the above study(SRC). Adsorption to particulate matter was not significant(1).
[(1) Duff PB; Proc of the SPI Tech/Mark Conf 29: 9-14 (1985)]**PEER REVIEWED**

Volatilization from Water/Soil:

The vapor pressure of TDI is 0.01 torr at 20 deg C(1), and therefore spilled TDI will not readily volatilize from soil surfaces or other surfaces(SRC). Since TDI reacts with water, volatilization from water should not be important(SRC).
[(1) IARC Monograph on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. 39: 287-323 (1985)]**PEER REVIEWED**

Environmental Water Concentrations:

Toluene diisocyanate has been reported in the waste-water of a furniture manufacturing area in a concn range of 0.1-4.1 mg/l.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 299 (1986)]**PEER REVIEWED**

Effluent Concentrations:

TDI has been reported in waste water from furniture manufacturing in the concn range of 0.1-4.1 ppm(1). However the coloremetric method used did not distinguish between the disocyanate or the corresponding amine(1). In view of TDI's rapid reactivity with water, it is probable that the chemical detected was the corresponding amine(SRC). Stack exhaust from a polyurethane foam production plant were reported to contain 100-17,700 ug/cu m of TDI(1).
[(1) IARC Monograph on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. 39: 287-323 (1985)]**PEER REVIEWED**

Sediment/Soil Concentrations:

Ten days after an accident resulting in the spillage of 13 tons of **toluene** diisocyanate from a lorry on a swampy wet forest area, **toluene** diisocyanate and toluenediamine were /found/ in the soil. After six yr,

only **toluene** diisocyanate-derived polyureas were found in soil samples taken at the same site.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 299 (1986)]**PEER REVIEWED**

Other Environmental Concentrations:

TDI monomer has been found in a urethane foam fabric coating in concn of <200 ppm(1).
[(1) IARC Monograph on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. 39: 287-323 (1985)]**PEER REVIEWED**

TOLUENE DIISOCYANATE

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For other data, click on the Table of Contents

Effluent Concentrations:

TDI has been reported in waste water from furniture manufacturing in the concn range of 0.1-4.1 ppm(1). However the coloremetric method used did not distinguish between the disocyanate or the corresponding amine(1). In view of TDI's rapid reactivity with water, it is probable that the chemical detected was the corresponding amine(SRC). Stack exhaust from a polyurethane foam production plant were reported to contain 100-17,700 ug/cu m of TDI(1).

[(1) IARC Monograph on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. 39: 287-323 (1985)]**PEER REVIEWED**

TOLUENE DIISOCYANATE

CASRN: 26471-62-5

For other data, click on the Table of Contents

Other Environmental Concentrations:

TDI monomer has been found in a urethane foam fabric coating in concn of <200 ppm(1).
[(1) IARC Monograph on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. 39: 287-323 (1985)]**PEER REVIEWED**

TOLUENE DIISOCYANATE

CASRN: 26471-62-5

For other data, click on the Table of Contents

Environmental Standards & Regulations:

TSCA Requirements:

Pursuant to section 8(d) of TSCA, EPA promulgated a model Health and Safety Data Reporting Rule. The section 8(d) model rule requires manufacturers, importers, and processors of listed chemical substances and mixtures to submit to EPA copies and lists of unpublished health and safety studies. Benzene, 1,3-diisocyanatomethyl- is included on this list.
[40 CFR 716.120 (7/1/91)]**PEER REVIEWED**

CERCLA Reportable Quantities:

Persons in charge of vessels or facilities are required to notify the National Response Center (NRC) immediately, when there is a release of this designated hazardous substance, in an amount equal to or greater than its reportable quantity of 100 lb or 45.4 kg. The toll free number of the NRC is (800) 424-8802; In the Washington D.C. metropolitan area (202) 426-2675. The rule for determining when notification is required is stated in 40 CFR 302.4 (section IV. D.3.b).
[40 CFR 302.4 (7/1/91)]**PEER REVIEWED**

RCRA Requirements:

U223; As stipulated in 40 CFR 261.33, when **toluene** diisocyanate, as a commercial chemical product or manufacturing chemical intermediate or an off-specification commercial chemical product or a manufacturing chemical intermediate, becomes a waste, it must be managed according to Federal and/or State hazardous waste regulations. Also defined as a hazardous waste is any residue, contaminated soil, water, or other debris resulting from the cleanup of a spill, into water or on dry land, of this waste. Generators of small quantities of this waste may qualify for partial exclusion from hazardous waste regulations (40 CFR 261.5).
[40 CFR 261.33 (7/1/91)]**PEER REVIEWED**

Atmospheric Standards:

This action promulgates standards of performance for equipment leaks of Volatile Organic Compounds (VOC) in the Synthetic Organic Chemical Manufacturing Industry (SOCMI). The intended effect of these standards is to require all newly constructed, modified, and reconstructed SOCMI process units to use the best demonstrated system of continuous emission reduction for equipment leaks of VOC, considering costs, non air quality health and environmental impact and energy requirements. **Toluene** diisocyanate is produced, as an intermediate or a final product, by process units covered under this subpart.
[40 CFR 60.489 (7/1/91)]**PEER REVIEWED**

TOLUENE DIISOCYANATE

CASRN: 26471-62-5

For other data, click on the Table of Contents

TSCA Requirements:

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[40 CFR 716.120 (7/1/91)]**PEER REVIEWED**

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For other data, click on the Table of Contents

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[40 CFR 302.4 (7/1/91)]**PEER REVIEWED**

TOLUENE DIISOCYANATE

CASRN: 26471-62-5

For other data, click on the Table of Contents

Chemical/Physical Properties:

Molecular Formula:

C9-H6-N2-O2
PEER REVIEWED

Color/Form:

Clear colorless to pale yellow liquid.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, D.C.: Assoc. of American Railroads,Hazardous Materials Systems (BOE), 1987. 686]**PEER REVIEWED**

Odor:

Pungent odor
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, D.C.: Assoc. of American Railroads,Hazardous Materials Systems (BOE), 1987. 686]**PEER REVIEWED**

Boiling Point:

251 deg C
[ITC/USEPA; Information Review #231 (Draft) Toluene Diisocyanates p.2 (1981)]**PEER REVIEWED**

Melting Point:

11-14 deg C (freezing point)
[Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984.,p. V15 790 (1981)]**PEER REVIEWED**

Density/Specific Gravity:

1.22 + or - 0.01 g/ml at 25 deg C
[ITC/USEPA; Information Review #231 (Draft) Toluene Diisocyanates p.2 (1981)]**PEER REVIEWED**

Spectral Properties:

Refractive Index 1.5666 at 25 deg C (80:20 mix); 1.5663 at 25 deg C (65:35 mixture)
[Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes

1-26. New York, NY: John Wiley and Sons, 1978-1984.,p. V15 790 (1981)]**PEER REVIEWED**

Vapor Pressure:

0.01 torr at 20 deg C
[IARC Monograph on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. 39: 287-323 (1985)]**PEER REVIEWED**

Other Chemical/Physical Properties:

VAPOR PRESSURE: 0.5 MM @ 25 DEG C /80% 2,4:20% 2,6/
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values, 4th ed., 1980. Cincinnati, Ohio: American Conference ofGovernmmental Industrial Hygienists, Inc., 1980. 401]**PEER REVIEWED**

MISCIBLE WITH ALCOHOL, ETHER, ACETONE /80% 2,4:20% 2,6/
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values, 4th ed., 1980. Cincinnati, Ohio: American Conference ofGovernmmental Industrial Hygienists, Inc., 1980. 401]**PEER REVIEWED**

MISCIBLE WITH CARBON TETRACHLORIDE /80% 2,4:20% 2,6/
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values, 4th ed., 1980. Cincinnati, Ohio: American Conference ofGovernmmental Industrial Hygienists, Inc., 1980. 401]**PEER REVIEWED**

MISCIBLE WITH BENZENE, KEROSENE /80% 2,4:20% 2,6/
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values, 4th ed., 1980. Cincinnati, Ohio: American Conference ofGovernmmental Industrial Hygienists, Inc., 1980. 401]**PEER REVIEWED**

SPECIFIC GRAVITY: 1.22 @ 25 DEG C; BP: 250 DEG C; FP: 11.3-13.5 DEG C /80% 2,4:20% 2,6/
[American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices. 5th ed. Cincinnati, OH:American Conference of Governmental Industrial Hygienists, 1986. 580]**PEER REVIEWED**

TOLUENE DIISOCYANATE

CASRN: 26471-62-5

For other data, click on the Table of Contents

Molecular Formula:

C9-H6-N2-O2

PEER REVIEWED

TOLUENE DIISOCYANATE

CASRN: 26471-62-5

For other data, click on the Table of Contents

Color/Form:

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[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, D.C.: Assoc. of American Railroads,Hazardous Materials Systems (BOE), 1987. 686]**PEER REVIEWED**

TOLUENE DIISOCYANATE

CASRN: 26471-62-5

For other data, click on the Table of Contents

Odor:

Pungent odor

[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, D.C.: Assoc. of American Railroads,Hazardous Materials Systems (BOE), 1987. 686]**PEER REVIEWED**

TOLUENE DIISOCYANATE

CASRN: 26471-62-5

For other data, click on the Table of Contents

Boiling Point:

251 deg C

[ITC/USEPA; Information Review #231 (Draft) Toluene Diisocyanates p.2 (1981)]**PEER REVIEWED**

TOLUENE DIISOCYANATE

CASRN: 26471-62-5

For other data, click on the Table of Contents

Melting Point:

11-14 deg C (freezing point)

[Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984.,p. V15 790 (1981)]**PEER REVIEWED**

TOLUENE DIISOCYANATE

CASRN: 26471-62-5

For other data, click on the Table of Contents

Density/Specific Gravity:

1.22 + or - 0.01 g/ml at 25 deg C

[ITC/USEPA; Information Review #231 (Draft) Toluene Diisocyanates p.2 (1981)]**PEER REVIEWED**

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[Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984.,p. V15 790 (1981)]**PEER REVIEWED**

TOLUENE DIISOCYANATE

CASRN: 26471-62-5

For other data, click on the Table of Contents

Vapor Pressure:

0.01 torr at 20 deg C

[IARC Monograph on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. 39: 287-323 (1985)]**PEER REVIEWED**

TOLUENE DIISOCYANATE

CASRN: 26471-62-5

For other data, click on the Table of Contents

Other Chemical/Physical Properties:

VAPOR PRESSURE: 0.5 MM @ 25 DEG C /80% 2,4:20% 2,6/
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values, 4th ed., 1980. Cincinnati, Ohio: American Conference ofGovernmmental Industrial Hygienists, Inc., 1980. 401]**PEER REVIEWED**

MISCIBLE WITH ALCOHOL, ETHER, ACETONE /80% 2,4:20% 2,6/
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values, 4th ed., 1980. Cincinnati, Ohio: American Conference ofGovernmmental Industrial Hygienists, Inc., 1980. 401]**PEER REVIEWED**

MISCIBLE WITH CARBON TETRACHLORIDE /80% 2,4:20% 2,6/
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values, 4th ed., 1980. Cincinnati, Ohio: American Conference ofGovernmmental Industrial Hygienists, Inc., 1980. 401]**PEER REVIEWED**

MISCIBLE WITH BENZENE, KEROSENE /80% 2,4:20% 2,6/
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values, 4th ed., 1980. Cincinnati, Ohio: American Conference ofGovernmmental Industrial Hygienists, Inc., 1980. 401]**PEER REVIEWED**

SPECIFIC GRAVITY: 1.22 @ 25 DEG C; BP: 250 DEG C; FP: 11.3-13.5 DEG C /80% 2,4:20% 2,6/
[American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices. 5th ed. Cincinnati, OH:American Conference of Governmental Industrial Hygienists, 1986. 580]**PEER REVIEWED**

TOLUENE DIISOCYANATE

CASRN: 26471-62-5

For other data, click on the Table of Contents

Chemical Safety & Handling:

DOT Emergency Guidelines:

Fire or explosion: Combustible material: may burn but does not ignite readily. Substance will react with water (some violently) releasing flammable, toxic or corrosive gases and runoff. When heated, vapors may form explosive mixtures with air: indoors, outdoors, and sewers explosion hazards. Most vapors are heavier than air. They will spread along ground and collect in low or confined areas (sewers, basements, tanks). Vapors may travel to source of ignition and flash back. Contact with metals may evolve flammable hydrogen gas. Containers may explode when heated or if contaminated with water.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-156]**QC REVIEWED**

Health: TOXIC; inhalation, ingestion or contact (skin, eyes) with vapors, dusts or substance may cause severe injury, burns, or death. Reaction with water or moist air will release toxic, corrosive or flammable gases. Reaction with water may generate much heat which will increase the concentration of fumes in the air. Fire will produce irritating, corrosive and/or toxic gases. Runoff from fire control or dilution water may be corrosive and/or toxic and cause pollution.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-156]**QC REVIEWED**

Public safety: CALL Emergency Response Telephone Number on Shipping Paper first. If Shipping Paper not available or no answer, refer to appropriate telephone number listed on the inside back cover. Isolate spill or leak area immediately for at least 50 to 100 meters (160 to 330 feet) in all directions. Keep unauthorized personnel away. Stay upwind. Keep out of low areas. Ventilate enclosed areas.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-156]**QC REVIEWED**

Protective clothing: Wear positive pressure self-contained breathing apparatus (SCBA). Wear chemical protective clothing which is specifically recommended by the manufacturer. Structural firefighters' protective clothing is recommended for fire situations ONLY; it is not effective in spill situations.

[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-156]**QC REVIEWED**

Evacuation: Spill: See the Table of Initial Isolation and Protective Action Distances for highlighted substances. For non-highlighted substances, increase, in the downwind direction, as necessary, the isolation distance shown under "PUBLIC SAFETY". Fire: If tank, rail car or tank truck is involved in a fire, ISOLATE for 800 meters (1/2 mile) in all directions; also, consider initial evacuation for 800 meters (1/2 mile) in all directions.

[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-156]**QC REVIEWED**

Fire: Note: Most foams will react with the material and release corrosive/toxic gases. Small fires: CO2, dry chemical, dry sand, alcohol-resistant foam. Large fires: Water spray, fog or alcohol-resistant foam. FOR CHLOROSILANES, DO NOT USE WATER; use AFFF alcohol-resistant medium expansion foam. Move containers from fire area if you can do it without risk. Do not use straight streams. Fire involving tanks or car/trailer loads: Fight fire from maximum distance or use unmanned hose holders or monitor nozzles. Do not get water inside containers. Cool containers with flooding quantities of water until well after fire is out. Withdraw immediately in case of rising sound from venting safety devices or discoloration of tank. ALWAYS stay away from the ends of tanks.

[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-156]**QC REVIEWED**

Spill or leak: ELIMINATE all ignition sources (no smoking, flares, sparks or flames in immediate area). All equipment used when handling the product must be grounded. Do not touch damaged containers or spilled material unless wearing appropriate protective clothing. Stop leak if you can do it without risk. A vapor suppressing foam may be used to reduce vapors. FOR CHLOROSILANES, use AFFF alcohol-resistant medium expansion foam to reduce vapors. DO NOT GET WATER on spilled substance or inside containers. Use water spray to reduce vapors or divert vapor cloud drift. Prevent entry into waterways, sewers, basements or confined areas. Small spills: Cover with DRY earth, DRY sand, or other non-combustible material followed with plastic sheet to minimize spreading or contact with rain. Use clean non-sparking tools to collect material and place it into loosely covered plastic containers for later disposal.

[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S.

Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-156]**QC REVIEWED**

First aid: Move victim to fresh air. Call emergency medical care. Apply artificial respiration if victim is not breathing. Do not use mouth-to-mouth method if victim ingested or inhaled the substance; induce artificial respiration with the aid of a pocket mask equipped with a one-way valve or other proper respiratory medical device. Administer oxygen if breathing is difficult. Remove and isolate contaminated clothing and shoes. In case of contact with substance, immediately flush skin or eyes with running water for at least 20 minutes. For minor skin contact, avoid spreading material on unaffected skin. Keep victim warm and quiet. Effects of exposure (inhalation, ingestion or skin contact) to substance may be delayed. Ensure that medical personnel are aware of the material(s) involved, and take precautions to protect themselves.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-156]**QC REVIEWED**

Odor Threshold:

Odor recognition in air: 2.10 ppm (purity)
[Fazzalari, F.A. (ed.). Compilation of Odor and Taste Threshold Values Data. ASTM Data Series DS 48A (Committee E-18). Philadelphia, PA: American Society for Testing and Materials, 1978. 158]**PEER REVIEWED**

TOLUENE DIISOCYANATE HAS MARKED CHARACTERISTIC ODOR WHICH ALLOWS IT TO BE DETECTED READILY. YET @ MAX RECOMMENDED CONCN (0.02 PPM) THE POISON CANNOT BE DETECTED BY ITS SMELL.
[Lefaux, R. Practical Toxicology of Plastics. Cleveland: CRC Press Inc., 1968. 102]**PEER REVIEWED**

Skin, Eye and Respiratory Irritations:

AS A VAPOR ... /**TOLUENE** DIISOCYANATE/ IS A POWERFUL IRRITANT TO EYES, SKIN, RESPIRATORY TRACT.
[Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984.,p. II-414]**PEER REVIEWED**

Fire Potential:

DUE TO ITS HIGH FLASH POINT, **TOLUENE** DIISOCYANATE OFFERS NO SERIOUS RISK OF FIRE ... .
[Lefaux, R. Practical Toxicology of Plastics. Cleveland: CRC Press Inc., 1968. 103]**PEER REVIEWED**

Combustible when exposed to heat or flame.
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 288 (1986)]**PEER REVIEWED**

Flash Point:

270 DEG F CLOSED CUP /80% 2,4:20% 2,6/
[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values, 4th ed., 1980. Cincinnati, Ohio: American Conference ofGovernmmental Industrial Hygienists, Inc., 1980. 401]**PEER REVIEWED**

132 deg C (open cup)
[Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984.,p. V15 791 (1981)]**PEER REVIEWED**

Fire Fighting Procedures:

FIREFIGHTERS MUST BE PROTECTED AGAINST DIISOCYANATE VAPORS & NO2 BY COMPLETE PROTECTIVE EQUIPMENT (CLOSED-CIRCUIT BREATHING APPARATUS, RUBBER GLOVES, ETC). /DIISOCYANATES/
[Lefaux, R. Practical Toxicology of Plastics. Cleveland: CRC Press Inc., 1968. 103]**PEER REVIEWED**

Firemen must be equipped with self-contained breathing apparatus. /Isocyanates/
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 1162]**PEER REVIEWED**

If material on fire or involved in fire: Do not extinguish fire unless flow can be stopped. Use water in flooding quantities as fog. Solid streams of water may be ineffective. Cool all affected containers with flooding quantities of water. Apply water from as far a distance as possible. Use "alcohol" foam, carbon dioxide, or dry chemical. Use water spray to knock-down vapors.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, D.C.: Assoc. of American Railroads,Hazardous Materials Systems (BOE), 1987. 686]**PEER REVIEWED**

Toxic Combustion Products:

Toxic oxides of nitrogen are produced during combustion of this material.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, D.C.: Assoc. of American Railroads,Hazardous Materials Systems (BOE), 1987. 686]**PEER REVIEWED**

Hazardous Reactivities & Incompatibilities:

It can react with aniline. The heat of this reaction may be sufficient to ignite surrounding combustibles and the material itself.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, D.C.: Assoc. of American Railroads,Hazardous Materials Systems (BOE), 1987. 686]**PEER REVIEWED**

Strong oxidizers, water, acids, bases and amines (may cause foam and splatter); alcohols. [Note: Reacts slowly with water to form carbon dioxide and polyureas.] /**Toluene** 2,4-diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

Hazardous Decomposition:

... WHEN HEATED TO DECOMPOSITION, IT EMITS HIGHLY TOXIC FUMES OF /HYDROGEN CHLORIDE AND NITROGEN OXIDES/.
[Sax, N.I. Dangerous Properties of Industrial Materials. 6th ed. New York, NY: Van Nostrand Reinhold, 1984. 2590]**PEER REVIEWED**

Immediately Dangerous to Life or Health:

NIOSH considers 2,4-**toluene** diisocyanate to be a potential occupational carcinogen. /2,4-**Toluene** diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

Protective Equipment & Clothing:

... Provide the workers with protective clothing, gloves and goggles. Respiratory protection may be provided by masks incorporating a prefilter, but the best form of protection in work carried on in a high concn of isocyanates is air-supplied breathing apparatus. /Isocyanates/
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 1162]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": ... dispensers of liq detergent /should be available./ ... Safety pipettes should be used for all pipetting. ... In animal laboratory, personnel should ... wear protective suits (preferably disposable, one-piece & close-fitting at ankles & wrists), gloves, hair covering & overshoes. ... In chemical laboratory, gloves & gowns should always be worn ... however, gloves should not be assumed to provide full protection. Carefully fitted masks or respirators may be necessary when working with particulates or gases, & disposable plastic aprons might provide addnl protection. ... Gowns ... /should be/ of distinctive color, this is a reminder that they are not to be worn outside the laboratory. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling

Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 8]**PEER REVIEWED**

Three commercial air-purifying respirators for protection against **toluene** diisocyanate vapors were evaluated. The Willson R-21 and Survivair, organic vapor cartridges, and the disposable, valveless 3M-8711 were the three respirators evaluated. Each respirator/cartridge was tested three times at 0.2 ppm **toluene** diisocyanate concn for 40 hr and once for 20 hr or more at concn greater than 1.5 ppm **toluene** diisocyanate. All cartridges/respirators had the capacity to provide the required protection against **toluene** diisocyanate vapors. Additional considerations in the respirator selection process included the training and experience of the respirator user, the enforcement of the respirator program, fit of the respirator, knowledge of **toluene** diisocyanate concn onsite, presence of other solvents or chemicals in the air which may adversely affect the capacity of the respirato for **toluene** diisocyanate, and the high odor threshold of **toluene** diisocyanate that makes it impossible for the user to receive advance warning of a leak.
[Dharmarajan V et al; Am Ind Hyg Assoc 47 (7): 393-8 (1986)]**PEER REVIEWED**

Wear appropriate eye protection to prevent eye contact. /**Toluene** 2,4-diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

Wear appropriate personal protective clothing to prevent skin contact. /**Toluene** 2,4-diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

Eyewash fountains should be provided in areas where there is any possibility that workers could be exposed to the substance; this is irrespective of the recommendation involving the wearing of eye protection. /**Toluene** 2,4-diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

Facilities for quickly drenching the body should be provided within the immediate work area for emergency use where there is a possibility of exposure. (Note: It is intended that these facilities provide a sufficient quantity or flow of water to quickly remove the substance from any body areas likely to be exposed. The actual determination of what constitutes an adequate quick drench facility depends on the specific circumstances. In certain instances, a deluge shower should be readily available, whereas in others, the availability of water from a sink or hose could be considered adequate.) /**Toluene** 2,4-diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

Recommendations for respirator selection: Condition: At concentrations above the NIOSH REL, or where there is no REL, at any detectable concentration: Respirator Class(es): Any self-contained

breathing apparatus that has a full facepiece and is operated in a pressure-demand or other positive pressure-mode. Any supplied-air respirator that has a full facepiece and is operated in a pressure-demand or other positive-pressure mode in combination with an auxiliary self-contained breathing apparatus operated in pressure-demand or other positive-pressure mode. /**Toluene** 2,4-diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

Recommendations for respirator selection: Escape from suddenly occurring respiratory hazards: Respirator Class(es): Any air-purifying, full-facepiece respirator (gas mask) with a chin-style, front- or back-mounted organic vapor canister. Any appropriate escape-type, self-contained breathing apparatus. /**Toluene** 2,4-diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

Preventive Measures:

VENTILATION SHOULD BE ADEQUATE ... OUTDOOR SPRAYING OPERATIONS SHOULD BE SHIELDED ... IF POLYURETHANE PRODUCTS ARE HEATED ... PROTECTION AGAINST ISOCYANATES THUS RELEASED IS NECESSARY. /ISOCYANATES/
[International Labour Office. Encyclopedia of Occupational Health and Safety. Volumes I and II. New York: McGraw-Hill Book Co., 1971. 746]**PEER REVIEWED**

The sanitary facilities ... /for/ workers must incl showers. /Isocyanates/
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 1162]**PEER REVIEWED**

If material not on fire and not involved in fire: Keep sparks, flames, and other sources of ignition away. Keep material out of water sources and sewers. Build dikes to contain flow as necessary. Attempt to stop leak if without hazard. Use water spray to knock-down vapors.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, D.C.: Assoc. of American Railroads,Hazardous Materials Systems (BOE), 1987. 686]**PEER REVIEWED**

Personnel protection: Avoid breathing vapors. Keep upwind. Avoid bodily contact with the material. Do not handle broken packages without protective equipment. Wash away any material which may have contacted the body with copious amounts of water or soap and water.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, D.C.: Assoc. of American Railroads,Hazardous Materials Systems (BOE), 1987. 686]**PEER REVIEWED**

Evacuation: If material leaking (not on fire), consider evacuation from downwind area based on amount of material spilled, location and weather conditions.

[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, D.C.: Assoc. of American Railroads,Hazardous Materials Systems (BOE), 1987. 686]**PEER REVIEWED**

SRP: Contaminated protective clothing should be segregated in such a manner so that there is no direct personal contact by personnel who handle, dispose, or clean the clothing. Quality assurance to ascertain the completeness of the cleaning procedures should be implemented before the decontaminated protective clothing is returned for reuse by the workers. Contaminated clothing should not be taken home at end of shift, but should remain at employee's place of work for cleaning.
PEER REVIEWED

PRECAUTIONS FOR "CARCINOGENS": Smoking, drinking, eating, storage of food or of food & beverage containers or utensils, & the application of cosmetics should be prohibited in any laboratory. All personnel should remove gloves, if worn, after completion of procedures in which carcinogens have been used. They should ... wash ... hands, preferably using dispensers of liq detergent, & rinse ... thoroughly. Consideration should be given to appropriate methods for cleaning the skin, depending on nature of the contaminant. No standard procedure can be recommended, but the use of organic solvents should be avoided. Safety pipettes should be used for all pipetting. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 8]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": In animal laboratory, personnel should remove their outdoor clothes & wear protective suits (preferably disposable, one-piece & close-fitting at ankles & wrists), gloves, hair covering & overshoes. ... Clothing should be changed daily but ... discarded immediately if obvious contamination occurs ... /also,/ workers should shower immediately. In chemical laboratory, gloves & gowns should always be worn ... however, gloves should not be assumed to provide full protection. Carefully fitted masks or respirators may be necessary when working with particulates or gases, & disposable plastic aprons might provide addnl protection. If gowns are of distinctive color, this is a reminder that they should not be worn outside of lab. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 8]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": ... Operations connected with synth & purification ... should be carried out under well-ventilated hood. Analytical procedures ... should be carried out with care & vapors evolved during ... procedures should be removed. ... Expert advice should be obtained before existing fume cupboards are used ... & when new fume cupboards are installed. It is desirable that there be means for decreasing the rate of air extraction, so that carcinogenic powders can be handled without ... powder being blown around the hood. Glove boxes should be kept under negative air pressure. Air changes should be adequate, so that concn of vapors of volatile carcinogens will not occur. /Chemical Carcinogens/

[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 8]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": Vertical laminar-flow biological safety cabinets may be used for containment of in vitro procedures ... provided that the exhaust air flow is sufficient to provide an inward air flow at the face opening of the cabinet, & contaminated air plenums that are under positive pressure are leak-tight. Horizontal laminar-flow hoods or safety cabinets, where filtered air is blown across the working area towards the operator, should never be used ... Each cabinet or fume cupboard to be used ... should be tested before work is begun (eg, with fume bomb) & label fixed to it, giving date of test & avg air-flow measured. This test should be repeated periodically & after any structural changes. /Chemical Carcinogens/

[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 9]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": Principles that apply to chem or biochem lab also apply to microbiological & cell-culture labs ... Special consideration should be given to route of admin. ... Safest method of administering volatile carcinogen is by injection of a soln. Admin by topical application, gavage, or intratracheal instillation should be performed under hood. If chem will be exhaled, animals should be kept under hood during this period. Inhalation exposure requires special equipment. ... unless specifically required, routes of admin other than in the diet should be used. Mixing of carcinogen in diet should be carried out in sealed mixers under fume hood, from which the exhaust is fitted with an efficient particulate filter. Techniques for cleaning mixer & hood should be devised before expt begun. When mixing diets, special protective clothing &, possibly, respirators may be required. /Chemical Carcinogens/

[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 9]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": When ... admin in diet or applied to skin, animals should be kept in cages with solid bottoms & sides & fitted with a filter top. When volatile carcinogens are given, filter tops should not be used. Cages which have been used to house animals that received carcinogens should be decontaminated. Cage-cleaning facilities should be installed in area in which carcinogens are being used, to avoid moving of ... contaminated /cages/. It is difficult to ensure that cages are decontaminated, & monitoring methods are necessary. Situations may exist in which the use of disposable cages should be recommended, depending on type & amt of carcinogen & efficiency with which it can be removed. /Chemical Carcinogens/

[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC

Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 10]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": To eliminate risk that ... contamination in lab could build up during conduct of expt, periodic checks should be carried out on lab atmospheres, surfaces, such as walls, floors & benches, & ... interior of fume hoods & airducts. As well as regular monitoring, check must be carried out after cleaning-up of spillage. Sensitive methods are required when testing lab atmospheres. ... Methods ... should ... where possible, be simple & sensitive. ... /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 10]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": Rooms in which obvious contamination has occurred, such as spillage, should be decontaminated by lab personnel engaged in expt. Design of expt should ... avoid contamination of permanent equipment. ... Procedures should ensure that maintenance workers are not exposed to carcinogens. ... Particular care should be taken to avoid contamination of drains or ventilation ducts. In cleaning labs, procedures should be used which do not produce aerosols or dispersal of dust, ie, wet mop or vacuum cleaner equipped with high-efficiency particulate filter on exhaust, which are avail commercially, should be used. Sweeping, brushing & use of dry dusters or mops should be prohibited. Grossly contaminated cleaning materials should not be re-used ... If gowns or towels are contaminated, they should not be sent to laundry, but ... decontaminated or burnt, to avoid any hazard to laundry personnel. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 10]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": Doors leading into areas where carcinogens are used ... should be marked distinctively with appropriate labels. Access ... limited to persons involved in expt. ... A prominently displayed notice should give the name of the Scientific Investigator or other person who can advise in an emergency & who can inform others (such as firemen) on the handling of carcinogenic substances. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 11]**PEER REVIEWED**

SRP: The scientific literature for the use of contact lenses in industry is conflicting. The benefit or detrimental effects of wearing contact lenses depend not only upon the substance, but also on factors including the form of the substance, characteristics and duration of the exposure, the uses of other eye protection equipment, and the hygiene of the lenses. However, there may be individual substances whose irritating or corrosive properties are such that the wearing of contact lenses would be harmful to the eye. In those specific cases, contact lenses should not be worn. In any event, the usual eye protection

equipment should be worn even when contact lenses are in place.
QC REVIEWED

The worker should immediately wash the skin when it becomes contaminated. /**Toluene** 2,4-diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

The worker should wash daily at the end of each work shift. /**Toluene** 2,4-diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

Work clothing that becomes wet or significantly contaminated should be removed and replaced. /**Toluene** 2,4-diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

Workers whose clothing may have become contaminated should change into uncontaminated clothing before leaving the work premises. /**Toluene** 2,4-diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

Shipment Methods and Regulations:

No person may /transport,/ offer or accept a hazardous material for transportation in commerce unless that person is registered in conformance ... and the hazardous material is properly classed, described, packaged, marked, labeled, and in condition for shipment as required or authorized by ... /the hazardous materials regulations (49 CFR 171-177)./
[49 CFR 171.2 (7/1/96)]**QC REVIEWED**

The International Air Transport Association (IATA) Dangerous Goods Regulations are published by the IATA Dangerous Goods Board pursuant to IATA Resolutions 618 and 619 and constitute a manual of industry carrier regulations to be followed by all IATA Member airlines when transporting hazardous materials.
[IATA. Dangerous Goods Regulations. 38th ed. Montreal, Canada and Geneva, Switzerland: International Air Transport Association, Dangerous Goods Board, January, 1997. 221]**QC REVIEWED**

The International Maritime Dangerous Goods Code lays down basic principles for transporting hazardous chemicals. Detailed recommendations for individual substances and a number of recommendations for good practice are included in the classes dealing with such substances. A general index of technical names has also been compiled. This index should always be consulted when attempting to locate the appropriate procedures to be used when shipping any substance or article.
[IMDG; International Maritime Dangerous Goods Code; International Maritime Organization p.6239 (1988)]**QC REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": Procurement ... of unduly large amt ... should be avoided. To avoid spilling, carcinogens should be transported in securely sealed glass bottles or ampoules, which should themselves be placed inside strong screw-cap or snap-top container that will not open when dropped & will resist attack from the carcinogen. Both bottle & the outside container should be appropriately labelled. ... National post offices, railway companies, road haulage companies & airlines have regulations governing transport of hazardous materials. These authorities should be consulted before ... material is shipped. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 13]**QC REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": When no regulations exist, the following procedure must be adopted. The carcinogen should be enclosed in a securely sealed, watertight container (primary container), which should be enclosed in a second, unbreakable, leakproof container that will withstand chem attack from the carcinogen (secondary container). The space between primary & secondary container should be filled with absorbent material, which would withstand chem attack from the carcinogen & is sufficient to absorb the entire contents of the primary container in the event of breakage or leakage. Each secondary container should then be enclosed in a strong outer box. The space between the secondary container & the outer box should be filled with an appropriate quantity of shock-absorbent material. Sender should use fastest & most secure form of transport & notify recipient of its departure. If parcel is not received when expected, carrier should be informed so that immediate effort can be made to find it. Traffic schedules should be consulted to avoid ... arrival on weekend or holiday ... /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 13]**QC REVIEWED**

Storage Conditions:

Store separated from amines, alcohols, bases and acids.
[Handling Chemicals Safely 1980; 2nd Ed, Dutch Association of Safety Experts, the Dutch Chemical Industry Association and the Dutch Institute: 970]**PEER REVIEWED**

Storage temp: 75-100 deg F
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": Storage site should be as close as practicable to lab in which carcinogens are to be used, so that only small quantities required for ... expt need to be carried. Carcinogens should be kept in only one section of cupboard, an explosion-proof refrigerator or freezer (depending on chemicophysical properties ...) that bears appropriate label. An inventory ... should be

kept, showing quantity of carcinogen & date it was acquired ... Facilities for dispensing ... should be contiguous to storage area. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 13]**PEER REVIEWED**

Cleanup Methods:

AQUEOUS SOLUTIONS CONTAINING 10-20% (WT) OF A NONIONIC SURFACTANT, ARKOPAL-N100, WAS A USEFUL DECONTAMINATING AGENT FOR TOLYLENE DIISOCYANATE (TDI). THE SOLUTION CAN BE SPRAYED DIRECTLY ON SPILLS AS A LIQUID OR MAY BE APPLIED IN THE FORM OF A FOAM WHICH CAN BE GENERATED IN SUITABLE FIRE EXTINGUISHING EQUIPMENT. SOLID DECONTAMINANT FORMULATIONS WERE ALSO DEVELOPED WHICH CAN BE USED FOR GROUND SPILLS OF TDI.
[IMPROVED DECONTAMINANT FOR TOLYLENE DIISOCYANATE (TDI); RES DISCL 193: 188 (1980)]**PEER REVIEWED**

Spillage: Neutralize with special mixt (50% water, 45% alc, 5% concn ammonia water), collect leaking liq in sealable containers (extra personal protection: self-contained breathing apparatus).
[Handling Chemicals Safely 1980; 2nd Ed, Dutch Association of Safety Experts, the Dutch Chemical Industry Association and the Dutch Institute: 970]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": A high-efficiency particulate arrestor (HEPA) or charcoal filters can be used to minimize amt of carcinogen in exhausted air ventilated safety cabinets, lab hoods, glove boxes or animal rooms ... Filter housing that is designed so that used filters can be transferred into plastic bag without contaminating maintenance staff is avail commercially. Filters should be placed in plastic bags immediately after removal ... The plastic bag should be sealed immediately ... The sealed bag should be labelled properly ... Waste liquids ... should be placed or collected in proper containers for disposal. The lid should be secured & the bottles properly labelled. Once filled, bottles should be placed in plastic bag, so that outer surface ... is not contaminated ... The plastic bag should also be sealed & labelled. ... Broken glassware ... should be decontaminated by solvent extraction, by chemical destruction, or in specially designed incinerators. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 15]**PEER REVIEWED**

Disposal Methods:

Generators of waste (equal to or greater than 100 kg/mo) containing this contaminant, EPA hazardous waste number U223, must conform with USEPA regulations in storage, transportation, treatment and disposal of waste.
[40 CFR 240-280, 300-306, 702-799 (7/1/91)]**PEER REVIEWED**

Toluene diisocyanate is a waste chemical stream constituent which may be subjected to ultimate disposal by controlled incineration. Controlled incineration: Oxides of nitrogen are removed from the effluent gas by scrubbers and/or thermal devices.
[USEPA; Engineering Handbook for Hazardous Waste Incineration p.2-10 (1981) EPA 68-03-3025]**PEER REVIEWED**

A potential candidate for rotary kiln incineration at a temperature range of 820 to 1,600 deg C and residence times of seconds for liquids and gases, and hours for solids. A potential candidate for liquid injection incineration at a temperature range of 650 to 1600 deg C and a residence time of 0.1 to 2 seconds. A potential candidate for fluidized bed incineration at a temperature range of 450 to 980 deg C and residence times of seconds for liquids and gases, and longer for solids.
[USEPA; Engineering Handbook for Hazardous Waste Incineration p.3-16 (1981) EPA 68-03-3025]**PEER REVIEWED**

This compound should be susceptible to removal from waste water by air stripping.
[USEPA/ORD; Innovative and Alternative Technology Assessment Manual pp.3-5, 3-11,12 (1980) EPA 430/9-78-009]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": There is no universal method of disposal that has been proved satisfactory for all carcinogenic compounds & specific methods of chem destruction ... published have not been tested on all kinds of carcinogen-containing waste. ... Summary of avail methods & recommendations ... /given/ must be treated as guide only. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 14]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": ... Incineration may be only feasible method for disposal of contaminated laboratory waste from biological expt. However, not all incinerators are suitable for this purpose. The most efficient type ... is probably the gas-fired type, in which a first-stage combustion with a less than stoichiometric air:fuel ratio is followed by a second stage with excess air. Some ... are designed to accept ... aqueous & organic-solvent solutions, otherwise it is necessary ... to absorb soln onto suitable combustible material, such as sawdust. Alternatively, chem destruction may be used, esp when small quantities ... are to be destroyed in laboratory. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 15]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": HEPA (high-efficiency particulate arrestor) filters ... can be disposed of by incineration. For spent charcoal filters, the adsorbed material can be stripped off at high temp & carcinogenic wastes generated by this treatment conducted to & burned in an incinerator. ... LIQUID WASTE: ... Disposal should be carried out by incineration at temp that ... ensure complete combustion. SOLID WASTE: Carcasses of lab animals, cage litter & misc solid wastes ... should be disposed of by incineration at temp high enough to ensure destruction of chem carcinogens or their

metabolites. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 15]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": ... Small quantities of ... some carcinogens can be destroyed using chem reactions ... but no general rules can be given. ... As a general technique ... treatment with sodium dichromate in strong sulfuric acid can be used. The time necessary for destruction ... is seldom known ... but 1-2 days is generally considered sufficient when freshly prepd reagent is used. ... Carcinogens that are easily oxidizable can be destroyed with milder oxidative agents, such as sat soln of potassium permanganate in acetone, which appears to be a suitable agent for destruction of hydrazines or of compounds containing isolated carbon-carbon double bonds. Concn or 50% aqueous sodium hypochlorite can also be used as an oxidizing agent. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 16]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": Carcinogens that are alkylating, arylating or acylating agents per se can be destroyed by reaction with appropriate nucleophiles, such as water, hydroxyl ions, ammonia, thiols & thiosulfate. The reactivity of various alkylating agents varies greatly ... & is also influenced by sol of agent in the reaction medium. To facilitate the complete reaction, it is suggested that the agents be dissolved in ethanol or similar solvents. ... No method should be applied ... until it has been thoroughly tested for its effectiveness & safety on material to be inactivated. For example, in case of destruction of alkylating agents, it is possible to detect residual compounds by reaction with 4(4-nitrobenzyl)-pyridine. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 17]**PEER REVIEWED**

TOLUENE DIISOCYANATE

CASRN: 26471-62-5

For other data, click on the Table of Contents

DOT Emergency Guidelines:

Fire or explosion: Combustible material: may burn but does not ignite readily. Substance will react with water (some violently) releasing flammable, toxic or corrosive gases and runoff. When heated, vapors may form explosive mixtures with air: indoors, outdoors, and sewers explosion hazards. Most vapors are heavier than air. They will spread along ground and collect in low or confined areas (sewers, basements, tanks). Vapors may travel to source of ignition and flash back. Contact with metals may evolve flammable hydrogen gas. Containers may explode when heated or if contaminated with water.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-156]**QC REVIEWED**

Health: TOXIC; inhalation, ingestion or contact (skin, eyes) with vapors, dusts or substance may cause severe injury, burns, or death. Reaction with water or moist air will release toxic, corrosive or flammable gases. Reaction with water may generate much heat which will increase the concentration of fumes in the air. Fire will produce irritating, corrosive and/or toxic gases. Runoff from fire control or dilution water may be corrosive and/or toxic and cause pollution.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-156]**QC REVIEWED**

Public safety: CALL Emergency Response Telephone Number on Shipping Paper first. If Shipping Paper not available or no answer, refer to appropriate telephone number listed on the inside back cover. Isolate spill or leak area immediately for at least 50 to 100 meters (160 to 330 feet) in all directions. Keep unauthorized personnel away. Stay upwind. Keep out of low areas. Ventilate enclosed areas.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-156]**QC REVIEWED**

Protective clothing: Wear positive pressure self-contained breathing apparatus (SCBA). Wear chemical protective clothing which is specifically recommended by the manufacturer. Structural firefighters' protective clothing is recommended for fire situations ONLY; it is not effective in spill situations.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the

Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-156]**QC REVIEWED**

Evacuation: Spill: See the Table of Initial Isolation and Protective Action Distances for highlighted substances. For non-highlighted substances, increase, in the downwind direction, as necessary, the isolation distance shown under "PUBLIC SAFETY". Fire: If tank, rail car or tank truck is involved in a fire, ISOLATE for 800 meters (1/2 mile) in all directions; also, consider initial evacuation for 800 meters (1/2 mile) in all directions.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-156]**QC REVIEWED**

Fire: Note: Most foams will react with the material and release corrosive/toxic gases. Small fires: CO2, dry chemical, dry sand, alcohol-resistant foam. Large fires: Water spray, fog or alcohol-resistant foam. FOR CHLOROSILANES, DO NOT USE WATER; use AFFF alcohol-resistant medium expansion foam. Move containers from fire area if you can do it without risk. Do not use straight streams. Fire involving tanks or car/trailer loads: Fight fire from maximum distance or use unmanned hose holders or monitor nozzles. Do not get water inside containers. Cool containers with flooding quantities of water until well after fire is out. Withdraw immediately in case of rising sound from venting safety devices or discoloration of tank. ALWAYS stay away from the ends of tanks.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-156]**QC REVIEWED**

Spill or leak: ELIMINATE all ignition sources (no smoking, flares, sparks or flames in immediate area). All equipment used when handling the product must be grounded. Do not touch damaged containers or spilled material unless wearing appropriate protective clothing. Stop leak if you can do it without risk. A vapor suppressing foam may be used to reduce vapors. FOR CHLOROSILANES, use AFFF alcohol-resistant medium expansion foam to reduce vapors. DO NOT GET WATER on spilled substance or inside containers. Use water spray to reduce vapors or divert vapor cloud drift. Prevent entry into waterways, sewers, basements or confined areas. Small spills: Cover with DRY earth, DRY sand, or other non-combustible material followed with plastic sheet to minimize spreading or contact with rain. Use clean non-sparking tools to collect material and place it into loosely covered plastic containers for later disposal.
[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training

(DHM-50), Washington, D.C. (1996).,p. G-156]**QC REVIEWED**

First aid: Move victim to fresh air. Call emergency medical care. Apply artificial respiration if victim is not breathing. Do not use mouth-to-mouth method if victim ingested or inhaled the substance; induce artificial respiration with the aid of a pocket mask equipped with a one-way valve or other proper respiratory medical device. Administer oxygen if breathing is difficult. Remove and isolate contaminated clothing and shoes. In case of contact with substance, immediately flush skin or eyes with running water for at least 20 minutes. For minor skin contact, avoid spreading material on unaffected skin. Keep victim warm and quiet. Effects of exposure (inhalation, ingestion or skin contact) to substance may be delayed. Ensure that medical personnel are aware of the material(s) involved, and take precautions to protect themselves.

[U.S. Department of Transportation. 1996 North American Emergency Response Guidebook. A Guidebook for First Responders During the Initial Phase of aHazardous Materials/Dangerous Goods Incident. U.S. Department of Transportation (U.S. DOT) Research and Special Programs Administration, Office of HazardousMaterials Initiatives and Training (DHM-50), Washington, D.C. (1996).,p. G-156]**QC REVIEWED**

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Odor Threshold:

Odor recognition in air: 2.10 ppm (purity)

[Fazzalari, F.A. (ed.). Compilation of Odor and Taste Threshold Values Data. ASTM Data Series DS 48A (Committee E-18). Philadelphia, PA: American Society for Testing and Materials, 1978. 158]**PEER REVIEWED**

TOLUENE DIISOCYANATE HAS MARKED CHARACTERISTIC ODOR WHICH ALLOWS IT TO BE DETECTED READILY. YET @ MAX RECOMMENDED CONCN (0.02 PPM) THE POISON CANNOT BE DETECTED BY ITS SMELL.

[Lefaux, R. Practical Toxicology of Plastics. Cleveland: CRC Press Inc., 1968. 102]**PEER REVIEWED**

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Fire Potential:

DUE TO ITS HIGH FLASH POINT, **TOLUENE** DIISOCYANATE OFFERS NO SERIOUS RISK OF FIRE ... .

[Lefaux, R. Practical Toxicology of Plastics. Cleveland: CRC Press Inc., 1968. 103]**PEER REVIEWED**

Combustible when exposed to heat or flame.

[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 288 (1986)]**PEER REVIEWED**

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Flash Point:

270 DEG F CLOSED CUP /80% 2,4:20% 2,6/

[American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values, 4th ed., 1980. Cincinnati, Ohio: American Conference ofGovernmmental Industrial Hygienists, Inc., 1980. 401]**PEER REVIEWED**

132 deg C (open cup)

[Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984.,p. V15 791 (1981)]**PEER REVIEWED**

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Fire Fighting Procedures:

FIREFIGHTERS MUST BE PROTECTED AGAINST DIISOCYANATE VAPORS & NO2 BY COMPLETE PROTECTIVE EQUIPMENT (CLOSED-CIRCUIT BREATHING APPARATUS, RUBBER GLOVES, ETC). /DIISOCYANATES/

[Lefaux, R. Practical Toxicology of Plastics. Cleveland: CRC Press Inc., 1968. 103]**PEER REVIEWED**

Firemen must be equipped with self-contained breathing apparatus. /Isocyanates/

[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 1162]**PEER REVIEWED**

If material on fire or involved in fire: Do not extinguish fire unless flow can be stopped. Use water in flooding quantities as fog. Solid streams of water may be ineffective. Cool all affected containers with flooding quantities of water. Apply water from as far a distance as possible. Use "alcohol" foam, carbon dioxide, or dry chemical. Use water spray to knock-down vapors.

[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, D.C.: Assoc. of American Railroads,Hazardous Materials Systems (BOE), 1987. 686]**PEER REVIEWED**

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Toxic Combustion Products:

Toxic oxides of nitrogen are produced during combustion of this material.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, D.C.: Assoc. of American Railroads,Hazardous Materials Systems (BOE), 1987. 686]**PEER REVIEWED**

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Hazardous Reactivities & Incompatibilities:

It can react with aniline. The heat of this reaction may be sufficient to ignite surrounding combustibles and the material itself.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, D.C.: Assoc. of American Railroads,Hazardous Materials Systems (BOE), 1987. 686]**PEER REVIEWED**

Strong oxidizers, water, acids, bases and amines (may cause foam and splatter); alcohols. [Note: Reacts slowly with water to form carbon dioxide and polyureas.] /**Toluene** 2,4-diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

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Hazardous Decomposition:

... WHEN HEATED TO DECOMPOSITION, IT EMITS HIGHLY TOXIC FUMES OF /HYDROGEN CHLORIDE AND NITROGEN OXIDES/.

[Sax, N.I. Dangerous Properties of Industrial Materials. 6th ed. New York, NY: Van Nostrand Reinhold, 1984. 2590]**PEER REVIEWED**

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Protective Equipment & Clothing:

... Provide the workers with protective clothing, gloves and goggles. Respiratory protection may be provided by masks incorporating a prefilter, but the best form of protection in work carried on in a high concn of isocyanates is air-supplied breathing apparatus. /Isocyanates/

[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 1162]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": ... dispensers of liq detergent /should be available./ ... Safety pipettes should be used for all pipetting. ... In animal laboratory, personnel should ... wear protective suits (preferably disposable, one-piece & close-fitting at ankles & wrists), gloves, hair covering & overshoes. ... In chemical laboratory, gloves & gowns should always be worn ... however, gloves should not be assumed to provide full protection. Carefully fitted masks or respirators may be necessary when working with particulates or gases, & disposable plastic aprons might provide addnl protection. ... Gowns ... /should be/ of distinctive color, this is a reminder that they are not to be worn outside the laboratory. /Chemical Carcinogens/

[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 8]**PEER REVIEWED**

Three commercial air-purifying respirators for protection against **toluene** diisocyanate vapors were evaluated. The Willson R-21 and Survivair, organic vapor cartridges, and the disposable, valveless 3M-8711 were the three respirators evaluated. Each respirator/cartridge was tested three times at 0.2 ppm **toluene** diisocyanate concn for 40 hr and once for 20 hr or more at concn greater than 1.5 ppm **toluene** diisocyanate. All cartridges/respirators had the capacity to provide the required protection against **toluene** diisocyanate vapors. Additional considerations in the respirator selection process included the training and experience of the respirator user, the enforcement of the respirator program, fit of the respirator, knowledge of **toluene** diisocyanate concn onsite, presence of other solvents or chemicals in the air which may adversely affect the capacity of the respirato for **toluene** diisocyanate, and the high odor threshold of **toluene** diisocyanate that makes it impossible for the user to receive advance warning of a leak.

[Dharmarajan V et al; Am Ind Hyg Assoc 47 (7): 393-8 (1986)]**PEER REVIEWED**

Wear appropriate eye protection to prevent eye contact. /**Toluene** 2,4-diisocyanate/

[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

Wear appropriate personal protective clothing to prevent skin contact. /**Toluene** 2,4-diisocyanate/

[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH)

Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

Eyewash fountains should be provided in areas where there is any possibility that workers could be exposed to the substance; this is irrespective of the recommendation involving the wearing of eye protection. /**Toluene** 2,4-diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

Facilities for quickly drenching the body should be provided within the immediate work area for emergency use where there is a possibility of exposure. (Note: It is intended that these facilities provide a sufficient quantity or flow of water to quickly remove the substance from any body areas likely to be exposed. The actual determination of what constitutes an adequate quick drench facility depends on the specific circumstances. In certain instances, a deluge shower should be readily available, whereas in others, the availability of water from a sink or hose could be considered adequate.) /**Toluene** 2,4-diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

Recommendations for respirator selection: Condition: At concentrations above the NIOSH REL, or where there is no REL, at any detectable concentration: Respirator Class(es): Any self-contained breathing apparatus that has a full facepiece and is operated in a pressure-demand or other positive pressure-mode. Any supplied-air respirator that has a full facepiece and is operated in a pressure-demand or other positive-pressure mode in combination with an auxiliary self-contained breathing apparatus operated in pressure-demand or other positive-pressure mode. /**Toluene** 2,4-diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

Recommendations for respirator selection: Escape from suddenly occurring respiratory hazards: Respirator Class(es): Any air-purifying, full-facepiece respirator (gas mask) with a chin-style, front- or back-mounted organic vapor canister. Any appropriate escape-type, self-contained breathing apparatus. /**Toluene** 2,4-diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

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Preventive Measures:

VENTILATION SHOULD BE ADEQUATE ... OUTDOOR SPRAYING OPERATIONS SHOULD BE SHIELDED ... IF POLYURETHANE PRODUCTS ARE HEATED ... PROTECTION AGAINST ISOCYANATES THUS RELEASED IS NECESSARY. /ISOCYANATES/
[International Labour Office. Encyclopedia of Occupational Health and Safety. Volumes I and II. New York: McGraw-Hill Book Co., 1971. 746]**PEER REVIEWED**

The sanitary facilities ... /for/ workers must incl showers. /Isocyanates/
[International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 1162]**PEER REVIEWED**

If material not on fire and not involved in fire: Keep sparks, flames, and other sources of ignition away. Keep material out of water sources and sewers. Build dikes to contain flow as necessary. Attempt to stop leak if without hazard. Use water spray to knock-down vapors.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, D.C.: Assoc. of American Railroads,Hazardous Materials Systems (BOE), 1987. 686]**PEER REVIEWED**

Personnel protection: Avoid breathing vapors. Keep upwind. Avoid bodily contact with the material. Do not handle broken packages without protective equipment. Wash away any material which may have contacted the body with copious amounts of water or soap and water.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, D.C.: Assoc. of American Railroads,Hazardous Materials Systems (BOE), 1987. 686]**PEER REVIEWED**

Evacuation: If material leaking (not on fire), consider evacuation from downwind area based on amount of material spilled, location and weather conditions.
[Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, D.C.: Assoc. of American Railroads,Hazardous Materials Systems (BOE), 1987. 686]**PEER REVIEWED**

SRP: Contaminated protective clothing should be segregated in such a manner so that there is no direct personal contact by personnel who handle, dispose, or clean the clothing. Quality assurance to ascertain the completeness of the cleaning procedures should be implemented before the decontaminated protective clothing is returned for reuse by the workers. Contaminated clothing should not be taken home at end of shift, but should remain at employee's place of work for cleaning.
PEER REVIEWED

PRECAUTIONS FOR "CARCINOGENS": Smoking, drinking, eating, storage of food or of food & beverage containers or utensils, & the application of cosmetics should be prohibited in any laboratory. All personnel should remove gloves, if worn, after completion of procedures in which carcinogens have been used. They should ... wash ... hands, preferably using dispensers of liq detergent, & rinse ... thoroughly. Consideration should be given to appropriate methods for cleaning the skin, depending on nature of the contaminant. No standard procedure can be recommended, but the use of organic solvents should be avoided. Safety pipettes should be used for all pipetting. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 8]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": In animal laboratory, personnel should remove their outdoor clothes & wear protective suits (preferably disposable, one-piece & close-fitting at ankles & wrists), gloves, hair covering & overshoes. ... Clothing should be changed daily but ... discarded immediately if obvious contamination occurs ... /also,/ workers should shower immediately. In chemical laboratory, gloves & gowns should always be worn ... however, gloves should not be assumed to provide full protection. Carefully fitted masks or respirators may be necessary when working with particulates or gases, & disposable plastic aprons might provide addnl protection. If gowns are of distinctive color, this is a reminder that they should not be worn outside of lab. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 8]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": ... Operations connected with synth & purification ... should be carried out under well-ventilated hood. Analytical procedures ... should be carried out with care & vapors evolved during ... procedures should be removed. ... Expert advice should be obtained before existing fume cupboards are used ... & when new fume cupboards are installed. It is desirable that there be means for decreasing the rate of air extraction, so that carcinogenic powders can be handled without ... powder being blown around the hood. Glove boxes should be kept under negative air pressure. Air changes should be adequate, so that concn of vapors of volatile carcinogens will not occur. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 8]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": Vertical laminar-flow biological safety cabinets may be used for containment of in vitro procedures ... provided that the exhaust air flow is sufficient to provide an inward air flow at the face opening of the cabinet, & contaminated air plenums that are under positive pressure are leak-tight. Horizontal laminar-flow hoods or safety cabinets, where filtered air is blown across the working area towards the operator, should never be used ... Each cabinet or fume cupboard to be used ... should be tested before work is begun (eg, with fume bomb) & label fixed to it, giving date of

test & avg air-flow measured. This test should be repeated periodically & after any structural changes. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 9]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": Principles that apply to chem or biochem lab also apply to microbiological & cell-culture labs ... Special consideration should be given to route of admin. ... Safest method of administering volatile carcinogen is by injection of a soln. Admin by topical application, gavage, or intratracheal instillation should be performed under hood. If chem will be exhaled, animals should be kept under hood during this period. Inhalation exposure requires special equipment. ... unless specifically required, routes of admin other than in the diet should be used. Mixing of carcinogen in diet should be carried out in sealed mixers under fume hood, from which the exhaust is fitted with an efficient particulate filter. Techniques for cleaning mixer & hood should be devised before expt begun. When mixing diets, special protective clothing &, possibly, respirators may be required. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 9]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": When ... admin in diet or applied to skin, animals should be kept in cages with solid bottoms & sides & fitted with a filter top. When volatile carcinogens are given, filter tops should not be used. Cages which have been used to house animals that received carcinogens should be decontaminated. Cage-cleaning facilities should be installed in area in which carcinogens are being used, to avoid moving of ... contaminated /cages/. It is difficult to ensure that cages are decontaminated, & monitoring methods are necessary. Situations may exist in which the use of disposable cages should be recommended, depending on type & amt of carcinogen & efficiency with which it can be removed. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 10]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": To eliminate risk that ... contamination in lab could build up during conduct of expt, periodic checks should be carried out on lab atmospheres, surfaces, such as walls, floors & benches, & ... interior of fume hoods & airducts. As well as regular monitoring, check must be carried out after cleaning-up of spillage. Sensitive methods are required when testing lab atmospheres. ... Methods ... should ... where possible, be simple & sensitive. ... /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for

Research on Cancer, 1979. 10]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": Rooms in which obvious contamination has occurred, such as spillage, should be decontaminated by lab personnel engaged in expt. Design of expt should ... avoid contamination of permanent equipment. ... Procedures should ensure that maintenance workers are not exposed to carcinogens. ... Particular care should be taken to avoid contamination of drains or ventilation ducts. In cleaning labs, procedures should be used which do not produce aerosols or dispersal of dust, ie, wet mop or vacuum cleaner equipped with high-efficiency particulate filter on exhaust, which are avail commercially, should be used. Sweeping, brushing & use of dry dusters or mops should be prohibited. Grossly contaminated cleaning materials should not be re-used ... If gowns or towels are contaminated, they should not be sent to laundry, but ... decontaminated or burnt, to avoid any hazard to laundry personnel. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 10]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": Doors leading into areas where carcinogens are used ... should be marked distinctively with appropriate labels. Access ... limited to persons involved in expt. ... A prominently displayed notice should give the name of the Scientific Investigator or other person who can advise in an emergency & who can inform others (such as firemen) on the handling of carcinogenic substances. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 11]**PEER REVIEWED**

SRP: The scientific literature for the use of contact lenses in industry is conflicting. The benefit or detrimental effects of wearing contact lenses depend not only upon the substance, but also on factors including the form of the substance, characteristics and duration of the exposure, the uses of other eye protection equipment, and the hygiene of the lenses. However, there may be individual substances whose irritating or corrosive properties are such that the wearing of contact lenses would be harmful to the eye. In those specific cases, contact lenses should not be worn. In any event, the usual eye protection equipment should be worn even when contact lenses are in place.
QC REVIEWED

The worker should immediately wash the skin when it becomes contaminated. /**Toluene** 2,4-diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

The worker should wash daily at the end of each work shift. /**Toluene** 2,4-diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing

Office, 1997. 313]**QC REVIEWED**

Work clothing that becomes wet or significantly contaminated should be removed and replaced. /**Toluene** 2,4-diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

Workers whose clothing may have become contaminated should change into uncontaminated clothing before leaving the work premises. /**Toluene** 2,4-diisocyanate/
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

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Shipment Methods and Regulations:

No person may /transport,/ offer or accept a hazardous material for transportation in commerce unless that person is registered in conformance ... and the hazardous material is properly classed, described, packaged, marked, labeled, and in condition for shipment as required or authorized by ... /the hazardous materials regulations (49 CFR 171-177)./

[49 CFR 171.2 (7/1/96)]**QC REVIEWED**

The International Air Transport Association (IATA) Dangerous Goods Regulations are published by the IATA Dangerous Goods Board pursuant to IATA Resolutions 618 and 619 and constitute a manual of industry carrier regulations to be followed by all IATA Member airlines when transporting hazardous materials.

[IATA. Dangerous Goods Regulations. 38th ed. Montreal, Canada and Geneva, Switzerland: International Air Transport Association, Dangerous Goods Board, January, 1997. 221]**QC REVIEWED**

The International Maritime Dangerous Goods Code lays down basic principles for transporting hazardous chemicals. Detailed recommendations for individual substances and a number of recommendations for good practice are included in the classes dealing with such substances. A general index of technical names has also been compiled. This index should always be consulted when attempting to locate the appropriate procedures to be used when shipping any substance or article.

[IMDG; International Maritime Dangerous Goods Code; International Maritime Organization p.6239 (1988)]**QC REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": Procurement ... of unduly large amt ... should be avoided. To avoid spilling, carcinogens should be transported in securely sealed glass bottles or ampoules, which should themselves be placed inside strong screw-cap or snap-top container that will not open when dropped & will resist attack from the carcinogen. Both bottle & the outside container should be appropriately labelled. ... National post offices, railway companies, road haulage companies & airlines have regulations governing transport of hazardous materials. These authorities should be consulted before ... material is shipped. /Chemical Carcinogens/

[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 13]**QC REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": When no regulations exist, the following procedure must be adopted. The carcinogen should be enclosed in a securely sealed, watertight container (primary container), which should be enclosed in a second, unbreakable, leakproof container that will withstand chem attack from the carcinogen (secondary container). The space between primary & secondary container should be filled with absorbent material, which would withstand chem attack from the carcinogen & is sufficient to absorb the entire contents of the primary container in the event of breakage or leakage. Each secondary container should then be enclosed in a strong outer box. The space between

the secondary container & the outer box should be filled with an appropriate quantity of shock-absorbent material. Sender should use fastest & most secure form of transport & notify recipient of its departure. If parcel is not received when expected, carrier should be informed so that immediate effort can be made to find it. Traffic schedules should be consulted to avoid ... arrival on weekend or holiday ... /Chemical Carcinogens/

[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 13]**QC REVIEWED**

TOLUENE DIISOCYANATE

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Storage Conditions:

Store separated from amines, alcohols, bases and acids.
[Handling Chemicals Safely 1980; 2nd Ed, Dutch Association of Safety Experts, the Dutch Chemical Industry Association and the Dutch Institute: 970]**PEER REVIEWED**

Storage temp: 75-100 deg F
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": Storage site should be as close as practicable to lab in which carcinogens are to be used, so that only small quantities required for ... expt need to be carried. Carcinogens should be kept in only one section of cupboard, an explosion-proof refrigerator or freezer (depending on chemicophysical properties ...) that bears appropriate label. An inventory ... should be kept, showing quantity of carcinogen & date it was acquired ... Facilities for dispensing ... should be contiguous to storage area. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 13]**PEER REVIEWED**

TOLUENE DIISOCYANATE

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Cleanup Methods:

AQUEOUS SOLUTIONS CONTAINING 10-20% (WT) OF A NONIONIC SURFACTANT, ARKOPAL-N100, WAS A USEFUL DECONTAMINATING AGENT FOR TOLYLENE DIISOCYANATE (TDI). THE SOLUTION CAN BE SPRAYED DIRECTLY ON SPILLS AS A LIQUID OR MAY BE APPLIED IN THE FORM OF A FOAM WHICH CAN BE GENERATED IN SUITABLE FIRE EXTINGUISHING EQUIPMENT. SOLID DECONTAMINANT FORMULATIONS WERE ALSO DEVELOPED WHICH CAN BE USED FOR GROUND SPILLS OF TDI. [IMPROVED DECONTAMINANT FOR TOLYLENE DIISOCYANATE (TDI); RES DISCL 193: 188 (1980)]**PEER REVIEWED**

Spillage: Neutralize with special mixt (50% water, 45% alc, 5% concn ammonia water), collect leaking liq in sealable containers (extra personal protection: self-contained breathing apparatus). [Handling Chemicals Safely 1980; 2nd Ed, Dutch Association of Safety Experts, the Dutch Chemical Industry Association and the Dutch Institute: 970]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": A high-efficiency particulate arrestor (HEPA) or charcoal filters can be used to minimize amt of carcinogen in exhausted air ventilated safety cabinets, lab hoods, glove boxes or animal rooms ... Filter housing that is designed so that used filters can be transferred into plastic bag without contaminating maintenance staff is avail commercially. Filters should be placed in plastic bags immediately after removal ... The plastic bag should be sealed immediately ... The sealed bag should be labelled properly ... Waste liquids ... should be placed or collected in proper containers for disposal. The lid should be secured & the bottles properly labelled. Once filled, bottles should be placed in plastic bag, so that outer surface ... is not contaminated ... The plastic bag should also be sealed & labelled. ... Broken glassware ... should be decontaminated by solvent extraction, by chemical destruction, or in specially designed incinerators. /Chemical Carcinogens/ [Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 15]**PEER REVIEWED**

TOLUENE DIISOCYANATE

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Disposal Methods:

Generators of waste (equal to or greater than 100 kg/mo) containing this contaminant, EPA hazardous waste number U223, must conform with USEPA regulations in storage, transportation, treatment and disposal of waste.
[40 CFR 240-280, 300-306, 702-799 (7/1/91)]**PEER REVIEWED**

Toluene diisocyanate is a waste chemical stream constituent which may be subjected to ultimate disposal by controlled incineration. Controlled incineration: Oxides of nitrogen are removed from the effluent gas by scrubbers and/or thermal devices.
[USEPA; Engineering Handbook for Hazardous Waste Incineration p.2-10 (1981) EPA 68-03-3025]**PEER REVIEWED**

A potential candidate for rotary kiln incineration at a temperature range of 820 to 1,600 deg C and residence times of seconds for liquids and gases, and hours for solids. A potential candidate for liquid injection incineration at a temperature range of 650 to 1600 deg C and a residence time of 0.1 to 2 seconds. A potential candidate for fluidized bed incineration at a temperature range of 450 to 980 deg C and residence times of seconds for liquids and gases, and longer for solids.
[USEPA; Engineering Handbook for Hazardous Waste Incineration p.3-16 (1981) EPA 68-03-3025]**PEER REVIEWED**

This compound should be susceptible to removal from waste water by air stripping.
[USEPA/ORD; Innovative and Alternative Technology Assessment Manual pp.3-5, 3-11,12 (1980) EPA 430/9-78-009]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": There is no universal method of disposal that has been proved satisfactory for all carcinogenic compounds & specific methods of chem destruction ... published have not been tested on all kinds of carcinogen-containing waste. ... Summary of avail methods & recommendations ... /given/ must be treated as guide only. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 14]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": ... Incineration may be only feasible method for disposal of contaminated laboratory waste from biological expt. However, not all incinerators are suitable for this purpose. The most efficient type ... is probably the gas-fired type, in which a first-stage combustion with a less than stoichiometric air:fuel ratio is followed by a second stage with excess air. Some ... are designed to accept ... aqueous & organic-solvent solutions, otherwise it is necessary ... to absorb soln onto suitable combustible material, such as sawdust. Alternatively, chem destruction may be used, esp when small quantities ... are to be destroyed in laboratory. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling

Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 15]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": HEPA (high-efficiency particulate arrestor) filters ... can be disposed of by incineration. For spent charcoal filters, the adsorbed material can be stripped off at high temp & carcinogenic wastes generated by this treatment conducted to & burned in an incinerator. ... LIQUID WASTE: ... Disposal should be carried out by incineration at temp that ... ensure complete combustion. SOLID WASTE: Carcasses of lab animals, cage litter & misc solid wastes ... should be disposed of by incineration at temp high enough to ensure destruction of chem carcinogens or their metabolites. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 15]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": ... Small quantities of ... some carcinogens can be destroyed using chem reactions ... but no general rules can be given. ... As a general technique ... treatment with sodium dichromate in strong sulfuric acid can be used. The time necessary for destruction ... is seldom known ... but 1-2 days is generally considered sufficient when freshly prepd reagent is used. ... Carcinogens that are easily oxidizable can be destroyed with milder oxidative agents, such as sat soln of potassium permanganate in acetone, which appears to be a suitable agent for destruction of hydrazines or of compounds containing isolated carbon-carbon double bonds. Concn or 50% aqueous sodium hypochlorite can also be used as an oxidizing agent. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 16]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": Carcinogens that are alkylating, arylating or acylating agents per se can be destroyed by reaction with appropriate nucleophiles, such as water, hydroxyl ions, ammonia, thiols & thiosulfate. The reactivity of various alkylating agents varies greatly ... & is also influenced by sol of agent in the reaction medium. To facilitate the complete reaction, it is suggested that the agents be dissolved in ethanol or similar solvents. ... No method should be applied ... until it has been thoroughly tested for its effectiveness & safety on material to be inactivated. For example, in case of destruction of alkylating agents, it is possible to detect residual compounds by reaction with 4(4-nitrobenzyl)-pyridine. /Chemical Carcinogens/
[Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory:Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. 17]**PEER REVIEWED**

TOLUENE DIISOCYANATE

CASRN: 26471-62-5

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Occupational Exposure Standards:

NIOSH Recommendations:

Experimental studies have demonstrated that **toluene** and TDA (a hydrolysis product of **toluene** diisocyanate) are carcinogens. The test results meet both OSHA and NIOSH criteria for classifying a substance as a potential occupational carcinogen. NIOSH therefore recommends that all isomers of **toluene** diisocyanate and TDA be considered as potential carcinogens and that exposures be limited to the lowest feasible concn.

[ANON; USDHHS, Public Health Service, Centers for Disease Control, NIOSH, Division of Standards Development and Technology Transfer, 4676 Columbia Parkway, Cincinnati OH 45226, USA, 1989. 20p. Bibl.]**PEER REVIEWED**

NIOSH considers 2,4-**toluene** diisocyanate to be a potential occupational carcinogen. /2,4-**Toluene** diisocyanate/

[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

NIOSH usually recommends that occupational exposures to carcinogens be limited to the lowest feasible concentration. /2,4-**Toluene** diisocyanate/

[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

Immediately Dangerous to Life or Health:

NIOSH considers 2,4-**toluene** diisocyanate to be a potential occupational carcinogen. /2,4-**Toluene** diisocyanate/

[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 313]**QC REVIEWED**

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Manufacturing/Use Information:

Major Uses:

POLYURETHANE FOAMS, ELASTOMERS AND COATINGS; CROSS-LINKING AGENT FOR NYLON-6

[Sax, N.I. and R.J. Lewis, Sr. (eds.). Hawley's Condensed Chemical Dictionary. 11th ed. New York: Van Nostrand Reinhold Co., 1987. 1163]**PEER REVIEWED**

POLYURETHANE ELASTOMERS MADE FROM **TOLUENE** DIISOCYANATES ARE USED IN COATED FABRICS & CLAY-PIPE SEALS. **TOLUENE** DIISOCYANATES ARE ALSO USED IN ADHESIVES OF POLYURETHANE & OTHER TYPES. /**TOLUENE** DIISOCYANATES/

[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V19 307 (1979)]**PEER REVIEWED**

POLYURETHANE COATINGS MADE FROM **TOLUENE** DIISOCYANATE MIXT ... IN GENERAL ... ARE USED IN FLOOR FINISHES, WOOD FINISHES & SEALERS, TRADE SALES PAINTS, CONCRETE SEALERS, & IN COATINGS FOR AIRCRAFT, TANK TRUCKS, TRUCK TRAILERS & TRUCK FLEETS. /MIXT OF 2,4- & 2,6-ISOMERS/

[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V19 307 (1979)]**PEER REVIEWED**

... used as hardener in the production of polyurethane.

[Maki-Paakkanen J, Norppa H; Toxicol Lett 36 (1): 37-43 (1987)]**PEER REVIEWED**

Manufacturers:

BASF Corporation, Chemicals Division, 1255 Broad St., Cliftn, NJ 07015, (201) 316-2937 /**Toluene** 2,4- and 2,6-diiscyanate (80/20) mixture/

[United States International Trade Commission. Synthetic Organic Chemicals-United States Production and Sales, 1991. USITC Publication 2607, February 1993.Washington, DC: United States Trade Commission, 1993.,p. 3-8]**PEER REVIEWED**

ICI Americas, Inc., Polyurethane Group 286 Manuta Grove Road, W. Deptford, NJ 08066-1732. (609) 423-8300; Speciality Product Division Concord Pike & Murphy Rd, Willmington, DE 19897, (302) 886-3000 /**Toluene** 2,4- and 2,6-diisocyanate (80/20) mixture/

[United States International Trade Commission. Synthetic Organic

Chemicals-United States Production and Sales, 1991. USITC Publication 2607, February 1993.Washington, DC: United States Trade Commission, 1993.,p. 3-8]**PEER REVIEWED**

Dow Chemical Co, 2020 Willard H. Dow Center, Midland, MI 48674, (517) 636-6125 /**Toluene** 2,4- and 2,6-diisocyanate (80/20) mixture/
[United States International Trade Commission. Synthetic Organic Chemicals-United States Production and Sales, 1991. USITC Publication 2607, February 1993.Washington, DC: United States Trade Commission, 1993.,p. 3-8]**PEER REVIEWED**

Olin Corporation, 120 Long Ridge Road, Stamford, CT 06904, (203) 356-2000 /**Toluene** 2,4- and 2,6-diisocyanate (80/20) mixture/
[United States International Trade Commission. Synthetic Organic Chemicals-United States Production and Sales, 1991. USITC Publication 2607, February 1993.Washington, DC: United States Trade Commission, 1993.,p. 3-8]**PEER REVIEWED**

Rubicon, Inc, PO Box 517, Geismar, LA 70734, (504) 673-6141 /**Toluene** 2,4- and 2,6-diisocyanate (80/20) mixture/
[United States International Trade Commission. Synthetic Organic Chemicals-United States Production and Sales, 1991. USITC Publication 2607, February 1993.Washington, DC: United States Trade Commission, 1993.,p. 3-8]**PEER REVIEWED**

Methods of Manufacturing:

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[CHEM & ENG NEWS 63 (37): 16 (1985)]**PEER REVIEWED**

From **toluene** diamine by reaction with carbonyl chloride (phosgene)
[Zenz, C. Occupational Medicine-Principles and Practical Applications. 2nd ed. St. Louis, MO: Mosby-Yearbook, Inc, 1988. 1016]**PEER REVIEWED**

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[CHEMICAL PRODUCTS SYNOPSIS: TOLUENE DIISOCYANATES, 1985]**PEER REVIEWED**

METHOD OF PURIFICATION: DISTILLATION TO REMOVE HYDROCHLORIC ACID.
[Sax, N.I. and R.J. Lewis, Sr. (eds.). Hawley's Condensed Chemical Dictionary. 11th ed. New York: Van Nostrand Reinhold Co., 1987. 1163]**PEER REVIEWED**

Formulations/Preparations:

GRADE: 100%-2,4 ISOMER; 80%:20%-2,4 & 2,6 ISOMER; 65%:35%-2,4 & 2,6 ISOMER
[Sax, N.I. and R.J. Lewis, Sr. (eds.). Hawley's Condensed Chemical Dictionary. 11th ed. New York: Van Nostrand Reinhold Co., 1987. 1163]**PEER REVIEWED**

Consumption Patterns:

90% FLEXIBLE FOAMS-MOLDED FLEXIBLE; 5% COATINGS; 3% ELASTOMERS; 2% OTHER (1984 EST) /FOR 80:20 MIX OF 2,4-2,6 ISOMER/
[CHEMICAL PRODUCTS SYNOPSIS: TOLUENE DIISOCYANATES, 1985]**PEER REVIEWED**

CHEMICAL PROFILE: **Toluene** Diisocyanate. Flexible urethane foams, 65%; (furniture, 28%; transportation, 16%; carpet underlay, 9%; bedding, 6%; other foam uses, 6%;) exports, 22%; rigid foams, 5%; polyurethane coatings, 4%; elastomers, 2%; miscellaneous non-foam uses, 2%.
[Kavaler AR; Chemical Marketing Reporter 232 (25): 50 (1987)]**PEER REVIEWED**

CHEMICAL PROFILE: **Toluene** diisocyanate. Demand: 1986: 650 million lb; 1987: 695 million lb; 1991 /projected/: 720 million lb (Includes exports, imports are negligible).
[Kavaler AR; Chemical Marketing Reporter 232 (25): 50 (1987)]**PEER REVIEWED**

80% 2,4:20% 2,6 MIXT REPRESENTS OVER 95% OF INDUSTRIAL USAGE ... .
[American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices. 5th ed. Cincinnati, OH:American Conference of Governmental Industrial Hygienists, 1986. 580]**PEER REVIEWED**

U. S. Production:

(1984) 3.32X10+11 g /80:20 MIX OF 2,4-2,6 ISOMERS/
[USITC. SYN ORG CHEM-U.S. PROD/SALES 1989 p.3-2]**PEER REVIEWED**

U. S. Imports:

(1983) 2.00X10+9 g /FOR 2,4 (AND 2,6) TDI/
[USITC. IMPORTS OF BENZENOID CHEMICALS & PRODUCTS 1983 p.29]**PEER REVIEWED**

(1983) 8.94X10+8 g /FOR TDI (UNMIXED)/
[USITC. IMPORTS OF BENZENOID CHEMICALS & PRODUCTS 1983 p.29]**PEER REVIEWED**

(1983) 2.00X10+7 g /2,4 TDI DIMER/
[USITC. IMPORTS OF BENZENOID CHEMICALS & PRODUCTS 1983 p.29]**PEER REVIEWED**

U. S. Exports:

(1984) 6.27x10+10 g /**TOLUENE** DIISOCYANATES/
[BUREAU OF THE CENSUS. U.S. EXPORTS (1984) p.2-73]**PEER REVIEWED**

TOLUENE DIISOCYANATE

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... used as hardener in the production of polyurethane.
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90% FLEXIBLE FOAMS-MOLDED FLEXIBLE; 5% COATINGS; 3% ELASTOMERS; 2% OTHER (1984 EST) /FOR 80:20 MIX OF 2,4-2,6 ISOMER/
[CHEMICAL PRODUCTS SYNOPSIS: TOLUENE DIISOCYANATES, 1985]**PEER REVIEWED**

CHEMICAL PROFILE: **Toluene** Diisocyanate. Flexible urethane foams, 65%; (furniture, 28%; transportation, 16%; carpet underlay, 9%; bedding, 6%; other foam uses, 6%;) exports, 22%; rigid foams, 5%; polyurethane coatings, 4%; elastomers, 2%; miscellaneous non-foam uses, 2%.
[Kavaler AR; Chemical Marketing Reporter 232 (25): 50 (1987)]**PEER REVIEWED**

CHEMICAL PROFILE: **Toluene** diisocyanate. Demand: 1986: 650 million lb; 1987: 695 million lb; 1991 /projected/: 720 million lb (Includes exports, imports are negligible).
[Kavaler AR; Chemical Marketing Reporter 232 (25): 50 (1987)]**PEER REVIEWED**

80% 2,4:20% 2,6 MIXT REPRESENTS OVER 95% OF INDUSTRIAL USAGE ... .
[American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices. 5th ed. Cincinnati, OH:American Conference of Governmental Industrial Hygienists, 1986. 580]**PEER REVIEWED**

TOLUENE DIISOCYANATE

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U. S. Production:

(1984) 3.32X10+11 g /80:20 MIX OF 2,4-2,6 ISOMERS/
[USITC. SYN ORG CHEM-U.S. PROD/SALES 1989 p.3-2]**PEER REVIEWED**

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U. S. Imports:

(1983) 2.00X10+9 g /FOR 2,4 (AND 2,6) TDI/
[USITC. IMPORTS OF BENZENOID CHEMICALS & PRODUCTS 1983 p.29]**PEER REVIEWED**

(1983) 8.94X10+8 g /FOR TDI (UNMIXED)/
[USITC. IMPORTS OF BENZENOID CHEMICALS & PRODUCTS 1983 p.29]**PEER REVIEWED**

(1983) 2.00X10+7 g /2,4 TDI DIMER/
[USITC. IMPORTS OF BENZENOID CHEMICALS & PRODUCTS 1983 p.29]**PEER REVIEWED**

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Analytic Laboratory Methods:

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[ALDER JF, ISAAC CA; ANAL CHIM ACTA 129 (1): 175 (1981)]**PEER REVIEWED**

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Matrix: Air. Sample preparation: Draw air through impinger containing aq acid; diazotize (NaNO2/NaBr); decompose excess nitrous acid; react with N-(1-naphthyl)-ethylenediamine. Procedure: colorimetric. Limit of detection: 50 ug/cu m. /From table/
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 300 (1986)]**PEER REVIEWED**

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[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International

Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 300 (1986)]**PEER REVIEWED**

Matrix: Air. Sample preparation: Draw air through impinger containing ethanol. Procedure: HPLC/UV. Limit of detection: 1-5 ug/cu m, /From table/
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer,1972-PRESENT. (Multivolume work).,p. V39 300 (1986)]**PEER REVIEWED**

Matrix: Air. Sample preparation: Draw air through impinger containing aq acid; neutralize; extract (chloroform or **toluene**); react with trifluoroacetic anhydride or heptafluorobutyric anhydride. Procedure: GC/ECD. Limit of detection: 1-5 ug/cu m. /From table/
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[U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. 5521-1]**PEER REVIEWED**

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High performance liquid chromatography, ultra violet detection. For 1-(2-methoxyphenyl)piperazine; NCO group, this method's estimated detection limit is not determined. The precision/RSD is 0.048 and the recovery is 96%. Applicability: This method determines the total concn of isocyanates, regardless of the identities of the specific cmpd present. Interferences: Phosgene, acid halides, and possibly some esters will react with 1-(2-methoxyphenyl)piperazine and thus cause a positive bias. /Isocyanate group/ [U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSHManual of Analytical Methods, 3rd ed. Volumes 1 and 2 with 1985 supplement, and revisions. Washington, DC: U.S. Government Printing Office, February 1984.,p. 5505-1]**PEER REVIEWED**

Isocyanate determination air paper tape Hydrazine determination air paper tape;Air analysis Hydrazine deriv. and **toluene** diisocyanate determination. in, miniature paper tape apparatus for [Hughes WT Jr; Anal Instrum (Research Triangle Park, N. C.) 22: 87-98 (1986)]**PEER REVIEWED**

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Special References:

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Davies RJ; Clinics in Immunology and Allergy 4 (1): 103-23 (1984) Respiratory Hypersensitivity To Diisocyanates

Kay S; Food and Chemical Toxicology 23 (3): 411-13. (1985) **Toluene** diisocyanate and Lung Function.

Toluene diisocyanate; Safety Practitioner 3 (5): 32-3 (1985).

DHHS/NTP; Toxicology & Carcinogenesis Studies of Commercial Grade 2,4 (80%)- and 2,6 (20%)-**Toluene** Diisocyanate in F344/N Rats and B6C3F1 Mice(Gavage Studies) Technical Report Series No. 251 (1986) NIH Publication No. 86-2507

U.S. Department of Health & Human Services/National Toxicology Program; 8th Report on Carcinogens. National Institute of Environmental Health Sciences, Research Triangle Park, NC. (1998)

... The toxicity of inhaled vapors of diisocyanates is summarized.
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Santodonato J et al; Report ISB SRC-TR-85-189 Order No PB86-180213/gar (1985)

Davies RJ; Clinics in Immunology and Allergy 4 (1): 103-23 (1984) Respiratory Hypersensitivity To Diisocyanates

Kay S; Food and Chemical Toxicology 23 (3): 411-13. (1985) **Toluene** diisocyanate and Lung Function.

Toluene diisocyanate; Safety Practitioner 3 (5): 32-3 (1985).

DHHS/NTP; Toxicology & Carcinogenesis Studies of Commercial Grade 2,4 (80%)- and 2,6 (20%)-**Toluene** Diisocyanate in F344/N Rats and B6C3F1 Mice(Gavage Studies) Technical Report Series No. 251 (1986) NIH Publication No. 86-2507

U.S. Department of Health & Human Services/National Toxicology Program; 8th Report on Carcinogens. National Institute of Environmental Health Sciences, Research Triangle Park, NC. (1998)

... The toxicity of inhaled vapors of diisocyanates is summarized.
[Davies RJ; Clinics in Immunology and Allergy 4 (1): 103-23 (1984)]

TOLUENE DIISOCYANATE

CASRN: 26471-62-5

For other data, click on the Table of Contents

Synonyms and Identifiers:

Related HSDB Records:

874 [2,4-**TOLUENE** DIISOCYANATE] (Mixture Component)

5272 [2,6-**TOLUENE** DIISOCYANATE] (Mixture Component)

Synonyms:

BENZENE, 1,3-DIISOCYANATOMETHYL-
PEER REVIEWED

DIISOCYANATOTOLUENE
PEER REVIEWED

HYLENE T
PEER REVIEWED

ISOCYANIC ACID, METHYL-M-PHENYLENE ESTER
PEER REVIEWED

METHYLPHENYLENE ISOCYANATE
PEER REVIEWED

METHYL-M-PHENYLENE ISOCYANATE
PEER REVIEWED

MONDUR TD
PEER REVIEWED

MONDUR TD-80
PEER REVIEWED

TDI
PEER REVIEWED

TOLYLENE DIISOCYANATE
PEER REVIEWED

TOLYLENE ISOCYANATE
PEER REVIEWED

Formulations/Preparations:

GRADE: 100%-2,4 ISOMER; 80%:20%-2,4 & 2,6 ISOMER; 65%:35%-2,4 & 2,6 ISOMER
[Sax, N.I. and R.J. Lewis, Sr. (eds.). Hawley's Condensed Chemical

Dictionary. 11th ed. New York: Van Nostrand Reinhold Co., 1987. 1163]**PEER REVIEWED**

Shipping Name/ Number DOT/UN/NA/IMO:

UN 2078; **Toluene** diisocyanate

IMO 6.1; **Toluene** diisocyanate

Standard Transportation Number:

49 215 75; **Toluene** diisocyanate

EPA Hazardous Waste Number:

U223; A toxic waste when a discarded commercial chemical product or manufacturing chemical intermediate or an off-specification commercial chemical product or a manufacturing chemical intermediate.

RTECS Number:

NIOSH/NQ9490000

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For other data, click on the Table of Contents

Administrative Information:

Hazardous Substances Databank Number: 6003

Last Revision Date: 20000929

Last Review Date: Reviewed by SRP on 9/24/1992

Update History:

Complete Update on 02/11/2000, 1 field added/edited/deleted.
Complete Update on 02/02/2000, 1 field added/edited/deleted.
Complete Update on 09/21/1999, 1 field added/edited/deleted.
Complete Update on 08/24/1999, 5 fields added/edited/deleted.
Complete Update on 06/03/1998, 1 field added/edited/deleted.
Complete Update on 03/16/1998, 3 fields added/edited/deleted.
Field Update on 05/01/1997, 2 fields added/edited/deleted.
Complete Update on 02/28/1997, 1 field added/edited/deleted.
Complete Update on 09/04/1996, 1 field added/edited/deleted.
Complete Update on 05/14/1996, 1 field added/edited/deleted.
Complete Update on 03/19/1996
Complete Update on 01/31/1996, 1 field added/edited/deleted.
Complete Update on 05/09/1995, 1 field added/edited/deleted.
Complete Update on 01/12/1995, 1 field added/edited/deleted.
Complete Update on 09/27/1994, 1 field added/edited/deleted.
Complete Update on 04/05/1994, 53 fields added/edited/deleted.
Field Update on 03/29/1994, 1 field added/edited/deleted.
Field Update on 04/30/1993, 1 field added/edited/deleted.
Field update on 01/11/1993, 1 field added/edited/deleted.
Field Update on 11/20/1992, 1 field added/edited/deleted.
Complete Update on 04/01/1992, 1 field added/edited/deleted.
Complete Update on 09/26/1991, 1 field added/edited/deleted.
Complete Update on 07/18/1991, 1 field added/edited/deleted.
Complete Update on 10/23/1990, 3 fields added/edited/deleted.
Field Update on 08/23/1990, 1 field added/edited/deleted.
Field Update on 05/04/1990, 1 field added/edited/deleted.
Complete Update on 04/13/1989, 2 fields added/edited/deleted.
Field Update on 03/01/1989, 1 field added/edited/deleted.
Complete Update on 12/28/1988, 83 fields added/edited/deleted.
Complete Update on 10/03/1986

Record Length: 225484

TOLUENE DIISOCYANATE

CASRN: 26471-62-5

For other data, click on the Table of Contents

Hazardous Substances Databank Number: 6003

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Complete Update on 06/03/1998, 1 field added/edited/deleted.
Complete Update on 03/16/1998, 3 fields added/edited/deleted.
Field Update on 05/01/1997, 2 fields added/edited/deleted.
Complete Update on 02/28/1997, 1 field added/edited/deleted.
Complete Update on 09/04/1996, 1 field added/edited/deleted.
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