RESIDUES OF FIRE ACCELERANT CHEMICALS

VOLUME II: LITERATURE SEARCH

Prepared for:

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LITERATURE SEARCH: RESIDUES OF FIRE ACCELERANT CHEMICALS

Structure of Report

This report presents the results of a literature search designed to identify data points for a quantitative risk assessment of the residues remaining after the use of fire accelerants to ignite prescribed burns.

Table 1, Chemicals List, presents the fire accelerants, their chemical components, and the residues expected to remain following combustion. Each of the following sections present the literature search for one of the residues, consisting of a table of data parameters followed by abstracts or summaries of the literature cited for that chemical.

The residues evaluated are as follows:

Table 1-1. Chemicals Evaluated in Risk Assessment

Accelerant	Components	Residues*
Fusee	Strontium nitrate + Potassium perchlorate + Sulfur + Sawdust/oil binder	Strontium sulfate Strontium oxide Strontium sulfide *Nitrogen oxides* Potassium chloride Potassium hydroxide *Carbon dioxide* *Water vapor* *Sulfur dioxide*
Gasoline	Gasoline mixture + MTBE (additive)	Gasoline as a mixture MTBE
Diesel fuel	Diesel fuel mixture	Diesel fuel as a mixture
Firegel/Alumagel/Suregel/ Petrol Jel	Aluminum carboxylates	Aluminum oxide *Water vapor*
Ping-pong balls	Potassium permanganate + Ethylene glycol + Polystyrene ball	Manganese dioxide Potassium hydroxide *Carbon dioxide* *Water vapor* *Styrene* Uncombusted polystyrene
Flares propelled by launcher pistols	Aluminum + Calcium sulfate + Iron oxide + Copper oxide + Silicon + Potassium perchlorate + Lead oxide + Black powder: (Potassium nitrate + Sulfur + Charcoal)	Aluminum Aluminum oxide Calcium sulfate Iron oxide Copper oxide Silicon dioxide Potassium chloride *Carbon dioxide* *Water vapor* Lead Potassium hydroxide *Nitrogen oxides* *Sulfur dioxide*
Propane	Propane	*Carbon dioxide* *Water vapor*

*Gaseous compounds are presented in italics; they are not analyzed in this assessment.
Sources: Etiumsoft 2002, Lewis 1994a, Lewis 1994b, Sumi and Tsuchiya 1971.

Free aluminum is reactive. Following combustion, aluminum oxide will be the dominant form.

Aluminum Oxide, CAS #1344-28-1 (Al_2O_3, aluminum trioxide, alumina)

Data Point	Data Summary	Reference
Water solubility	Practically insoluble 0.000098 g/100 cc = 0.0000098 mg/L	Budavari et al. 1989 ATSDR 1999
K_{oc}		
Soil half-life	No degradation.	ATSDR 1999
BCF	BCFs are less than 300 in fish, since aluminum is highly toxic to fish species.	ATSDR 1999
Ingestion toxicity	A minimal risk level of 2.0 mg/kg/day was estimated for intermediate (15 to 364 days) oral exposure, based on the most sensitive toxicity endpoint (neurotoxicity) identified in studies in laboratory animals.	ATSDR 1999
Carcinogenicity	Chronic ingestion studies in mice and rats using aluminum potassium sulfate or aluminum phosphide led reviewers to conclude that aluminum has not demonstrated carcinogenicity in laboratory animals.	ATSDR 1999
Mammalian tox	Oral LD_{50}s are 162 and 164 mg/kg in rat and mouse, respectively.	ATSDR 1999
Avian tox	14-day LD_{50} >8,000 mg/kg in northern bobwhite and 4,997 in Japanese quail for monoethyl ester phosphonic acid aluminum salt (CAS # 39148-24-8), equivalent to >2,303 and 1,439 mg Al_2O_3/kg, respectively.	EPA 2002
Fish toxicity	96-hour LC_{50} in rainbow trout = 0.310 mg Al/L, equal to 1.17 mg Al_2O_3/L	EPA 2002
Aq. invert. tox	24-hour LC_{50}s in water fleas (Daphnia spp.) were 2.6 and 3.5 mg/L	EPA 2002
Aq. amph. tox	96-hour LC_{50} for aluminum in Jefferson salamander embryos is approximately 0.38 mg/L, equivalent to 1.4 mg Al_2O_3/L LC_{10} (NOEC) was 0.3 mg/L, 24-hour LC_{50} was 0.5 mg/L, LC_{100} was 0.7 mg/L for aluminum in common toad embryos 7-day LC_{50} for aluminum in eastern narrowmouth toad embryo-larvae was 0.05 mg/L	Pauli et al. 2000

Agency for Toxic Substances and Disease Registry. 1999. Toxicological profile for aluminum. Atlanta, GA. http://www.atsdr.cdc.gov/toxprofiles/tp22.html

ATSDR. See Agency for Toxic Substances and Disease Registry.

Budavari, S., M.J. O'Neil, A. Smith, and P.E. Heckelman, eds. 1989. *The Merck Index: An Encyclopedia of Chemicals, Drugs, and Biologicals.* Merck and Co., Inc. Rahway, NJ.

EPA. See U.S. Environmental Protection Agency.

Pauli, B.D., J.A. Perrault, and S.L. Money. 2000. RATL: A database of reptile and amphibian toxicology literature. Technical Report Series No. 357. Canadian Wildlife Service, Headquarters, Hull, Québec, Canada. http://www.cws-scf.ec.gc.ca/nwrc/ratl/about_e.htm

U.S. Environmental Protection Agency. 2002. Ecotox database: Aluminum. Mid-Continent Ecology Division, National Health and Environmental Effects Research Laboratory, Office of Research and Development. Duluth, MN. http://www.epa.gov/ecotox/

Agency for Toxic Substances and Disease Registry. 1999. Toxicological profile for aluminum. Atlanta, GA.

Report summarized by ATSDR in the form of ToxFAQs document; relevant sections follow:

ToxFAQs™ for Aluminum, CAS# 7429-90-5, June 1999

HIGHLIGHTS: Everyone is exposed to low levels of aluminum from food, air, and water. Exposure to high levels of aluminum may result in respiratory problems.

Aluminum occurs naturally and makes up about 8% of the surface of the earth. It is always found combined with other elements such as oxygen, silicon, and fluorine.

What happens to aluminum when it enters the environment? It binds to particles in the air. It can dissolve in lakes, streams, and rivers depending on the quality of the water. Acid rain may dissolve aluminum from soil and rocks. It can be taken up into some plants from soil. It is not known to bioconcentrate up the food chain.

How might I be exposed to aluminum? Eating small amounts of aluminum in food. Breathing higher levels of aluminum dust in workplace air. Drinking water with high levels of aluminum near waste sites, manufacturing plants, or areas naturally high in aluminum. Eating substances containing high levels of aluminum (such as antacids) especially when eating or drinking citrus products at the same time. Very little enters your body from aluminum cooking utensils.

How can aluminum affect my health? Low-level exposure to aluminum from food, air, water, or contact with skin is not thought to harm your health. Aluminum, however, is not a necessary substance for our bodies and too much may be harmful. People who are exposed to high levels of aluminum in air may have respiratory problems including coughing and asthma from breathing dust. Some studies show that people with Alzheimer's disease have more aluminum than usual in their brains. We do not know whether aluminum causes the disease or whether the buildup of aluminum happens to people who already have the disease. Infants and adults who received large doses of aluminum as a treatment for another problem developed bone diseases, which suggests that aluminum may cause skeletal problems. Some sensitive people develop skin rashes from using aluminum chlorohydrate deodorants.

How likely is aluminum to cause cancer? The Department of Health and Human Services, the International Agency for Research on Cancer, and the EPA have not classified aluminum for carcinogenicity. Aluminum has not been shown to cause cancer in animals.

How does aluminum affect children? Children with kidney problems who were given aluminum in their medical treatments developed bone diseases. Other health effects of aluminum on children have not been studied. It is not known whether aluminum affects children differently than adults, or what the long-term effects might be in adults exposed as children. Large amounts of aluminum have been shown to be harmful to unborn and developing animals because it can cause delays in skeletal and neurological development. Aluminum has been shown to cause lower birthweights in some animals.

Budavari, S., M.J. O'Neil, A. Smith, and P.E. Heckelman, eds. 1989. *The Merck Index: An Encyclopedia of Chemicals, Drugs, and Biologicals.* Merck and Co., Inc. Rahway, NJ.

359. Aluminum Oxide. Alumina. Al_2O_3; mol wt 101.94. Al 52.91%, O 47.08%. Occurs in nature as the minerals: **bauxite, bayerite, boehmite, corundum, diaspore, gibbsite**. Prepn and properties: *Mellor's* vol. V, 263-273 (1929); *Gmelin's. Aluminum* (8^{th} ed.) **35B**, pp 7-98 (1934); Becher in *Handbook of Preparative Inorganic Chemistry* vol. 1, G. Grauer. Ed. (Academic Press, New York, 2^{nd} ed., 1963) pp 822-823; Wagner, *ibid*. vol. 2 (1965) pp 1660-1663.

Approximate characteristics of native aluminum oxide: White cryst powder. d^{20}_4 4.0 mp about 2000°. Very hard, about 8.8 on Moh's scale. An electrical insulator; electrical resistivity at 300° about 1.2×10^{13} ohms-cm. Practically insol in water. Slowly sol in aq alkaline solns with the formation of hydroxides. Practically insol in non-polar organic solvents.

USE: As adsorbent, dessicant, abrasive; as filler for paints and varnishes; in manuf of alloys, ceramic materials, electrical insulators and resistors, dental cements, glass, steel, artificial gems; in coatings for metals, etc.; as catalyst for organic reactions. The minerals *corundum* (hardness = 9) and ***Alundium*** (obtained by fusing bauxite in an electric furnace) are used as abrasives and polishes; in manuf of refractories. Aluminum oxide is also used in chromatography , *see* Aluminum Oxide (Brockmann).

Pauli, B.D., J.A. Perrault, and S.L. Money. 2000. RATL: A database of reptile and amphibian toxicology literature. Technical Report Series No. 357. Canadian Wildlife Service, Headquarters, Hull, Québec, Canada.

> The RATL (Reptile and Amphibian Toxicology Literature) database contains data extracted from the primary literature for amphibian and reptile ecotoxicology studies published up to and including 1997; there are some data from studies published in 1998 and 1999. As of September, 2000, there was approximately 2000 references in the database. Citations were gathered through searches of various literature databases, but these searches concentrated on the environmental pollution literature with the result that the bibliography cannot be considered exhaustive.

U.S. Environmental Protection Agency. 2002. Ecotox database: Aluminum. Mid-Continent Ecology Division, National Health and Environmental Effects Research Laboratory, Office of Research and Development. Duluth, MN.

The ECOTOXicology database is a source for locating single chemical toxicity data for aquatic life, terrestrial plants and wildlife. ECOTOX integrates three toxicology effects databases: AQUIRE (aquatic life), PHYTOTOX (terrestrial plants), and TERRETOX (terrestrial wildlife). These databases were created by the U.S. EPA, Office of Research and Development (ORD), and the National Health and Environmental Effects Research Laboratory (NHEERL), Mid-Continent Ecology Division.

Scientific name, Common name	**End-point**	**Effect**	**Trend --- Effect %**	**Media Type**	**Duration --- Exp Typ**	**Conc (ug/L)**	**Signif --- Level**	**Response Site --- BCF**	**Ref #**
Daphnia magna Water flea	LC50	MOR	--------	FW	24 H ----------	F 3500		------	3936
Daphnia pulex Water flea	LC50	MOR	--------	FW	24 H ----------	F 2600		------	3936
Oncorhynchus mykiss Rainbow trout,donaldson trout	LC50	MOR	INC --------	FW	96 H ---------- S	T 310		------	14405

Calcium Sulfate, CAS #7778-18-9 ($CaSO_4$, plaster of Paris, gypsum)

Data Point	Data Summary	Reference
Water solubility	3,000 mg/L	HSDB 2002
K_{oc}	No data.	
Soil half-life	Stable. Naturally occurring compound as gypsum.	HSDB 2002
BCF	No data.	
Ingestion toxicity	Substance added directly to human food affirmed as generally recognized as safe (GRAS).	21 CFR 184.1230
Carcinogenicity	Inhalation of calcium sulfate fibers resulted in tumors in laboratory animals.	HSDB 2002
Fish toxicity	96-hour LC_{50} in bluegill sunfish >2,980 mg/L	EPA 2002
Aq. invert. tox	24-hour LC_{50} in water flea *Daphnia magna* >1,970 mg/L	EPA 2002
Aq. amph. tox	No data.	

21 CFR 184.1230. Direct food substances affirmed as Generally Recognized as Safe--Listing of Specific Substances Affirmed as GRAS. Calcium sulfate. U.S. Food and Drug Administration.

EPA. See U.S. Environmental Protection Agency.

Hazardous Substances Databank. 2002. On-line database. National Library of Medicine. Bethesda, MD. http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB

HSDB. See Hazardous Substances Databank.

U.S. Environmental Protection Agency. 2002. Ecotox database: Calcium sulfate. Mid-Continent Ecology Division, National Health and Environmental Effects Research Laboratory, Office of Research and Development. Duluth, MN. http://www.epa.gov/ecotox/

21 CFR 184.1230. Direct food substances affirmed as Generally Recognized as Safe--Listing of Specific Substances Affirmed as GRAS. Calcium sulfate. U.S. Food and Drug Administration.

TITLE 21--FOOD AND DRUGS
CHAPTER I--FOOD AND DRUG ADMINISTRATION, DEPARTMENT OF HEALTH AND HUMAN SERVICES (CONTINUED)

PART 184--DIRECT FOOD SUBSTANCES AFFIRMED AS GENERALLY RECOGNIZED AS SAFE--
Table of Contents
Subpart B--Listing of Specific Substances Affirmed as GRAS
Sec. 184.**1230** Calcium sulfate.

(a) Calcium sulfate (CaSO<INF>4,</INF> CAS Reg. No. 7778-18-9 or CaSO<INF>4</INF><t-bullet>2H<INF>2</INF>O, CAS Reg. No. 10101-41-4), also known as plaster of Paris, anhydrite, and gypsum, occurs naturally and exists as a fine, white to slightly yellow-white odorless powder. The anhydrous form is prepared by complete dehydration of gypsum, below 300 deg.C, in an electric oven.

(b) The ingredient meets the specifications of the ``Food Chemicals Codex,'' 3d Ed. (1981), p. 66, which is incorporated by reference. Copies may be obtained from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) The ingredient is used as an anticaking agent as defined in Sec. 170.3(o)(1) of this chapter, color and coloring adjunct as defined in Sec. 170.3(o)(4) of this chapter, dough strengthener as defined in Sec. 170.3(o)(6) of this chapter, drying agent as defined in Sec. 170.3(o)(7) of this chapter, firming agent as defined in Sec. 170.3(o)(10) of this chapter, flour treating agent as defined in Sec. 170.3(o)(13) of this chapter, formulation aid as defined in Sec. 170.3(o)(14) of this chapter, leavening agent as defined in Sec. 170.3(o)(17) of this chapter, nutrient supplement as defined in Sec. 170.3(o)(20) of this chapter, pH control agent as defined in Sec. 170.3(o)(23) of this chapter, processing aid as defined in Sec. 170.3(o)(24) of this chapter, stabilizer and thickener as defined in Sec. 170.3(o)(28) of this chapter, synergist as defined in Sec. 170.3(o)(31) of this chapter, and texturizer as defined in Sec. 170.3(o)(32) of this chapter.

(d) The ingredient is used in food at levels not to exceed good manufacturing practice in accordance with Sec. 184.1(b)(1). Current good manufacturing practice results in a maximum level, as served, of 1.3 percent for baked goods as defined in Sec. 170.3(n)(1) of this chapter, 3.0 percent for confections and frostings as defined in Sec. 170.3(n)(9) of this chapter, 0.5 percent for frozen dairy desserts and mixes as defined in Sec. 170.3(n)(20) of this chapter, 0.4 percent for gelatins and puddings as defined in Sec. 170.3(n)(22) of this chapter, 0.5 percent for grain products and pastas as defined in Sec. 170.3(n)(23) of this chapter, 0.35 percent for processed vegetables as defined in Sec. 170.3(n)(36) of this chapter, and 0.07 percent or less for all other food categories.

(e) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.
[45 FR 6086, Jan. 25, 1980; 45 FR 26319, Apr. 18, 1980, as amended at 49 FR 5611, Feb. 14, 1984]

Hazardous Substances Databank. 2002. On-line database. National Library of Medicine. Bethesda, MD.

HSDB is a toxicology data file on the National Library of Medicine's (NLM) Toxicology Data Network (TOXNET®). It focuses on the toxicology of potentially hazardous chemicals. It is enhanced with information on human exposure, industrial hygiene, emergency handling procedures, environmental fate, regulatory requirements, and related areas. All data are referenced and derived from a core set of books, government documents, technical reports and selected primary journal literature. HSDB is peer-reviewed by the Scientific Review Panel (SRP), a committee of experts in the major subject areas within the data bank's scope. HSDB is organized into individual chemical records, and contains over 4500 such records.

The following are the human health and environmental fate summaries from HSDB:

Human Health Effects:

Human Toxicity Excerpts:

GYPSUM DUST HAS AN IRRITANT ACTION ON MUCOUS MEMBRANES OF THE RESPIRATORY TRACT & EYES, & THERE HAVE BEEN REPORTS OF CONJUNCTIVITIS, CHRONIC RHINITIS, LARYNGITIS, PHARYNGITIS, IMPAIRED SENSE OF SMELL & TASTE, BLEEDING FROM THE NOSE, & REACTIONS OF TRACHEAL & BRONCHIAL MEMBRANES IN EXPOSED WORKERS. /GYPSUM/
[International Labour Office. Encyclopedia of Occupational Health and Safety. Volumes I and II. New York: McGraw-Hill Book Co., 1971. 630]**PEER REVIEWED**

Because it hardens quickly after absorbing moisture, its ingestion may result in obstruction, particularly at the pylorus. ... To delay "setting," drink glycerin or gelatin solutions, or large volumes of water. Surgical relief may be necessary. /Plaster of Paris/
[Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984.,p. II-127]**PEER REVIEWED**

... Calcium sulfate caused no lung disease in calcium sulfate miners.
[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. 204]**PEER REVIEWED**

Medical Surveillance:

IT IS ADVISABLE FOR GYPSUM & GYPSUM-PRODUCTS WORKERS TO RECEIVE A PRE-EMPLOYMENT EXAMINATION FOLLOWED BY PERIODIC EXAMINATIONS EACH YR. /GYPSUM/
[International Labour Office. Encyclopedia of Occupational Health and Safety. Volumes I and II. New York: McGraw-Hill Book Co., 1971. 630]**PEER REVIEWED**

Probable Routes of Human Exposure:

WORKERS EMPLOYED IN PROCESSING OF GYPSUM ROCK MAY BE EXPOSED TO HIGH ATMOSPHERIC CONCN OF GYPSUM DUST ... FURNACE GASES & SMOKE. IN GYPSUM CALCINATING, WORKERS ARE EXPOSED TO HIGH ENVIRONMENTAL TEMP, & THERE IS ALSO THE HAZARD OF BURNS. /GYPSUM/
[International Labour Office. Encyclopedia of Occupational Health and Safety. Volumes I and II. New York: McGraw-Hill Book Co., 1971. 630]**PEER REVIEWED**

Environmental Fate & Exposure:

Natural Pollution Sources:

NATURAL FORM OF ANHYDROUS CALCIUM SULFATE IS KNOWN AS MINERAL ANHYDRITE; ALSO AS KARSTENITE, MURIACITE, ANHYDROUS SULFATE OF LIME, ANHYDROUS GYPSUM.
[The Merck Index. 9th ed. Rahway, New Jersey: Merck & Co., Inc., 1976. 216]**PEER REVIEWED**

MINERAL WITH CHEM COMPOSITION CASO4.2H2O. ... IT IS RARELY FOUND PURE & GYPSUM DEPOSITS MAY CONTAIN QUARTZ, PYRITES, CARBONATES & CLAYEY & BITUMINOUS MATERIALS. IT OCCURS IN NATURE IN 5 VARIETIES: GYPSUM ROCK; GYPSITE ... ALABASTER ... SATIN SPAR ... & SELENITE. /GYPSUM/
[International Labour Office. Encyclopedia of Occupational Health and Safety. Volumes I and II. New York: McGraw-Hill Book Co., 1971. 630]**PEER REVIEWED**

Calcium sulfate is the commonest of the natural sulfates.
[Harben PW, Bates RL; Geology of the Nonmetallics p.237 (1984)]**PEER REVIEWED**

Domestic resources are adequate but are unevenly distributed. There are no gypsum deposits on the eastern seaboard of the United States. Large deposits occur in the Great Lakes region, mid-continent region, California, and other States. /Gypsum/
[BUREAU OF MINES. MINERAL COMMODITY SUMMARIES 1986 p.67]**PEER REVIEWED**

U.S. Environmental Protection Agency. 2002. Ecotox database: Calcium sulfate. Mid-Continent Ecology Division, National Health and Environmental Effects Research Laboratory, Office of Research and Development. Duluth, MN.

The ECOTOXicology database is a source for locating single chemical toxicity data for aquatic life, terrestrial plants and wildlife. ECOTOX integrates three toxicology effects databases: AQUIRE (aquatic life), PHYTOTOX (terrestrial plants), and TERRETOX (terrestrial wildlife). These databases were created by the U.S. EPA, Office of Research and Development (ORD), and the National Health and Environmental Effects Research Laboratory (NHEERL), Mid-Continent Ecology Division.

Scientific name, Common name	Endpoint	Effect	Trend --------- Effect %	Media Type	Duration ---------- Exp Typ	Conc (ug/L)	Signif ------- Level	Response Site ------- BCF	Ref #
Daphnia magna Water flea	LC50	MOR	INC --------	FW	24 H ---------- S	T >1970000, >1970000 - >1970000		------	18272
Lepomis macrochirus Bluegill	LC50	MOR	INC --------	FW	96 H ---------- S	T 2980000		------	5683

Copper Oxide, CAS #1317-38-0

Data Point	Data Summary	Reference
Water solubility	Practically insoluble. In its Cu(II) state, copper forms coordination compounds or complexes with both inorganic and organic ligands. At the pH values and carbonate concentrations characteristic of natural waters, most dissolved Cu(II) exists as carbonate complexes rather than as free (hydrated) cupric ions.	HSDB 2002 ATSDR 1990
K_{oc}	No data	
Soil half-life	Copper is a stable element. Copper oxide may form complexes with soil or dissolve in water, depending on the pH and organic carbon content of the specific soil.	
BCF	The bioconcentration factor (BCF) of copper in fish obtained in field studies is 10- 100, indicating a low potential for bioconcentration.	ATSDR 1990
Ingestion toxicity	The mean daily dietary intake of copper in adults ranges between 0.9 and 2.2 mg 300 mg Cu/kg/day was the LOAEL causing death in weanling rats when administered over a period of 2 to 15 weeks. Equivalent to 376 mg CuO/kg/day.	HSDB 2002
Carcinogenicity	Inadequate data to determine carcinogenicity.	EPA 1991
Avian toxicity	500 mg Cu/kg caused adverse effects in the domestic chicken, equivalent to 626 mg CuO/kg. No LD_{50} for avian species was identified.	Eisler 1998
Fish toxicity	The 96-hour LC_{50} for rainbow trout was 25.4 mg/L.	EPA 2002
Aq. invert. tox	The 48-hour EC_{50} for intoxication for the water flea *Daphnia magna* was 0.011 to 0.039 mg/L. The 48-hour EC_{50} for mortality in *Ceriodaphnia dubia* was 0.028 mg Cu/L = 0.035 mg CuO/L.	EPA 2002
Aq. amph. tox	No data.	

Agency for Toxic Substances and Disease Registry. 1990. Toxicological profile for copper. Atlanta, GA. http://www.atsdr.cdc.gov/toxprofiles/tp132.html

ATSDR. See Agency for Toxic Substances and Disease Registry.

Eisler, R. 1998. Copper hazards to fish, wildlife, and invertebrates: a synoptic review. Biological Science Report USGS/BRD/BSR--1998-0002. U.S. Geological Survey, Biological Resources Division. Laurel, MD. http://www.pwrc.usgs.gov/new/chrback.htm

EPA. See U.S. Environmental Protection Agency.

Hazardous Substances Databank. 2002. On-line database. National Library of Medicine. Bethesda, MD. http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB

HSDB. See Hazardous Substances Databank.

U.S. Environmental Protection Agency. 1991. Integrated risk information system. Office of Research and Development. Cincinnati, OH. http://www.epa.gov/iris/subst/0368.htm

U.S. Environmental Protection Agency. 2002. Ecotox database: Cupric oxide. Mid-Continent Ecology Division, National Health and Environmental Effects Research Laboratory, Office of Research and Development. Duluth, MN. http://www.epa.gov/ecotox/

Agency for Toxic Substances and Disease Registry. 1999. Toxicological profile for copper. Atlanta, GA.

Report summarized by ATSDR in the form of ToxFAQs document; relevant sections follow:

HIGHLIGHTS: Copper is an element that is found naturally in the environment. Small amounts of copper are necessary for good health; however, very large amounts can cause dizziness, headaches, diarrhea, and liver and kidney damage.

What happens to copper when it enters the environment? Copper is emitted to the air through natural processes such as windblown dust and volcanic eruptions. Human activities such as copper smelting and ore processing also result in copper being released to the air. Copper may enter the air when it is applied as a fungicide to plants, wood, fabric, and leather. Copper is released to water as a result of natural weathering of soil. It may also be released to water from discharges from industries and sewage treatment plants. Copper may also be added to lakes and ponds to control algae.

How can copper affect my health? Copper is necessary for good health. However, very large doses can be harmful. Long-term exposure to copper in the air can irritate your nose, mouth, and eyes, and cause dizziness, headaches, and diarrhea. Eating or drinking very high amounts of copper can cause liver and kidney damage and effects on the blood. Drinking water with higher than normal levels of copper can cause vomiting, diarrhea, stomach cramps, and nausea. Skin contact with copper can result in an allergic reaction in some people. This reaction is usually skin irritation or a skin rash. Animal studies have shown effects on the stomach and abnormalities in development when animals were fed a diet high in copper. Copper has not been shown to cause cancer in people or animals. The International Agency for Research on Cancer (IARC) has determined that copper is not classifiable as to human carcinogenicity.

The EPA has set a treatment technique for copper in drinking water that includes an action level of 1.3 milligrams of copper per liter of water (1.3 mg/L). The EPA has also set a secondary maximum contaminant level (SMCL) of 1 mg/L of copper in drinking water. An SMCL is a nonenforceable drinking water standard based on taste, odor, or other aesthetic considerations.

Hazardous Substances Databank. 2002. On-line database. National Library of Medicine. Bethesda, MD.

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The following are the human health and environmental fate summaries from HSDB:

Human Health Effects:

Toxicity Summary:

For healthy, non-occupationally-exposed humans the major route of exposure to copper is oral. The mean daily dietary intake of copper in adults ranges between 0.9 and 2.2 mg. ... In some cases, drinking water may make a substantial additional contribution to the total daily intake of copper, particularly in households where corrosive waters have stood in copper pipes. ... All other intakes of copper (inhalation and dermal) are insignificant in comparison to the oral route. Inhalation adds 0.3-2.0 ug/day from dusts and smoke. Women using copper IUDs are exposed to only 80ug or less of copper per day from this source. The homeostasis of copper involves the dual essentiality and toxicity of the element. Its essentiality arises from its specific incorporation into a large number of proteins for catalytic and structural purposes. The cellular pathways of uptake, incorporation into protein and export of copper are conserved in mammals and modulated by the metal itself. Copper is mainly absorbed through the gastrointestinal tract. From 20 to 60% of the dietary copper is absorbed, with the rest being excreted through the feces. Once the metal passes through the basolateral membrane it is transported to the liver bound to serum albumin. The liver is the critical organ for copper homeostatis. The copper is partitioned for excretion through the bile or incorporation into intra- and extracellular proteins. The primary route of excretion is through the bile. The transport of copper to the peripheral tissues is accomplished through the plasma attached to serum albumin, ceruloplasmin or low-molecular weight complexes. ... The biochemical toxicity of copper, when it exceeds homeostatic control, is derived from its effects on the structure and function of biomolecules, such as DNA, membranes and proteins directly or through oxygen-radical mechanisms. The toxicity of a single oral dose of copper varies widely between species. ... The major soluble salts (copper(II) sulfate, copper(II) chloride) are generally more toxic than the less soluble salts (copper(II) hydroxide, copper (II) oxide). Death is preceded by gastric hemorrhage, tachycardia, hypotension, hemolytic crisis, convulsions and paralysis. ... Long-term exposure in rats and mice showed no overt signs of toxicity other than a dose-related reduction in growth after ingestion ... The effects included inflammation of the liver and degeneration of kidney tubule epithelium. ... Some testicular degeneration and reduced neonatal body and organ weights were seen in rats ... and fetotoxic effects and malformations were seen at high dose levels. ... Neurochemical changes have been reported after oral administration ... A limited number of immunotoxicity studies showed humoral and cell-mediated immune function impairment in mice after oral intakes in drinking-water ... Copper is an essential element and adverse health effects /in humans/ are related to deficiency as well as excess. Copper deficiency is associated with anemia, neutropenia and bone abnormalities but clinically evident deficiency is relatively infrequent in humans. .. Except for occasional acute incidents of copper poisoning, few effects are noted in normal /human/ populations. Effects of single exposure following suicidal or accidental oral exposure have been reported as metallic taste, epigastric pain, headache, nausea, dizziness,

vomiting and diarrhea, tachycardia, respiratory difficulty, hemolytic anemia, hematuria, massive gastrointestinal bleeding, liver and kidney failure, and death. Gastrointestinal effects have also resulted from single and repeated ingestion of drinking-water containing high copper concentrations, and liver failure has been reported following chronic ingestion of copper. Dermal exposure has not been associated with systemic toxicity but copper may induce allergic responses in sensitive individuals. Metal fume fever from inhalation of high concentrations in the air in occupational settings have been reported ... A number of groups are described where apparent disorders in copper homeostasis result in greater sensitivity to copper deficit or excess than the general population. Some disorders have a well-defined genetic basis. These include Menkes disease, a generally fatal manifestation of copper deficiency; Wilson disease (hepatolenticular degeneration), a condition leading to progressive accumulation of copper; and hereditary aceruloplasminemia, with clinical symptoms of copper overload. Indian childhood cirrhosis and idiopathic copper toxicosis are conditions related to excess copper which may be associated with genetically based copper sensitivity ... These are fatal conditions in early childhood where copper accumulates in the liver. ... Other groups potentially sensitive to copper excess are hemodialysis patients and subjects with chronic liver disease. Groups at risk of copper deficiency include infants (particularly low birth weight/preterm babies, children recovering from malnutrition, and babies fed exclusively with cow's milk), people with maladsorption syndrome (e.g., celiac disease, sprue, cystic fibrosis), and patients on total parenteral nutrition. Copper deficiency has been implicated in the pathogenesis of cardiovascular disease. The adverse effects of copper must be balanced against its essentiality. Copper is an essential element for all biota ... At least 12 major proteins require copper as an integral part of their structure. It is essential for the utilization of iron in the formation of hemoglobin, and most crustaceans and molluscs possess the copper-containing hemocyanin as their main oxygen-carrying blood protein. ... A critical factor in assessing the hazard of copper is its bioavailablity. Adsorption of copper to particles and complexation by organic matter can greatly limit the degree to which copper will be accumulated ... At many sites, physiochemical factors limiting bioavailability will warrant higher copper limits. ...
[Environmental Health Criteria 200: Copper pp. 1-11 (1998) 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.]**PEER REVIEWED**

Environmental Fate & Exposure:

Probable Routes of Human Exposure:

Exposure may occur in copper and brass plants and during the welding of copper alloys.
[NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997. 76]**PEER REVIEWED**

Natural Pollution Sources:

OCCURS IN NATURE AS MINERALS TENORITE (TRICLINIC CRYSTALS) & PARAMELACONITE (TETRAHEDRAL, CUBIC CRYSTALS).
[The Merck Index. 10th ed. Rahway, New Jersey: Merck Co., Inc., 1983. 378]**PEER REVIEWED**

U.S. Environmental Protection Agency. 1991. Integrated risk information system. Office of Research and Development. Cincinnati, OH.

Status of Data for Copper

File First On-Line: 09/07/1988
Last Significant Revision: 09/07/1988
Category Status Last Revised
Oral RfD Assessment No data
Inhalation RfC Assessment No data
Carcinogenicity Assessment On-line 08/01/1991

Weight of Evidence (1986 US EPA Guidelines):
D (Not classifiable as to human carcinogenicity)

Weight of Evidence Narrative:
There are no human data, inadequate animal data from assays of copper compounds, and equivocal mutagenicity data.

This may be a synopsis of the full weight-of-evidence narrative. See Full IRIS Summary.

Quantitative Estimate of Carcinogenic Risk from Oral Exposure
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Not Assessed under the IRIS Program.

Quantitative Estimate of Carcinogenic Risk from Inhalation Exposure
---
Not Assessed under the IRIS Program.

U.S. Environmental Protection Agency. 2002. Ecotox database: Cupric oxide. Mid-Continent Ecology Division, National Health and Environmental Effects Research Laboratory, Office of Research and Development. Duluth, MN.

Scientific name, Common name	Endpoint	Effect	Trend --- Effect %	Media Type	Duration --- Exp Typ	Conc (ug/L)	Signif --- Level	Response Site --- BCF	Ref #
Daphnia magna Water flea	EC50	ITX	---	FW	48 H --- S	T 11 - 39		---	10917
Oncorhynchus mykiss Rainbow trout, donaldson trout	LC50	MOR	---	FW	96 H --- S	F 25.4, 21.8 - 29.5 ppm		---	344

Diesel Fuel, CAS #68334-30-5 (Diesel fuel no. 2)

Data Point	Data Summary	Reference
Water solubility	0.00076 mg/L.	TPHCWG 1997, 1998
K_{oc}	log K_{oc} is 6.7 (K_{oc} = 5,011,872)	TPHCWG 1997, 1998
Soil half-life	40% biodegradation in 28 days = $t_{1/2}$ of 21 days	Chevron 2001
BCF	Components of gas oil have measured or calculated log K_{ow} values in the range 3.9 to greater than 6, indicating a high potential to bioaccumulate. However there is little measured data on gas oils or their components and there are major technical difficulties in measuring bioconcentration (BCF) values with complex mixtures.	CONCAWE 1996
Ingestion toxicity	Oral LD_{50} in rats = 7,400 mg/kg Doses of 125+ mg/kg for five days increased the frequency of chromosomal aberrations in the bone marrow of Sprague-Dawley rats	API 1980a, as cited in CONCAWE 1996 WHO 1996
Carcinogenicity	Not classifiable as to carcinogenicity in humans	IARC 1989
Avian toxicity	Mallard LD_{50} = 20 mg/kg	NPS 1997
Fish toxicity	96-hour LC_{50} in rainbow trout is 21 to 210 mg/L 24-hour LC_{50}s were 1.40 to 1.97 for pink salmon, 26.7 to >55.6 for coho salmon, and >23.1 to 168.4 for rainbow trout.	Chevron 2001 WHO 1996
Aq. invert. tox	48-hour EC_{50} in *Daphnia magna* is 20 to 210 mg/L	Chevron 2001
Aq. amph. tox	96-hour LC_{50} for larvae of wood frog *Rana sylvatica* is 4.2 mg/L	Hedtke and Puglisi 1982, as cited in CONCAWE 1996

Chevron Products Co. 2001. Material safety data sheet 6894: Chevron LS diesel 2. San Ramon, CA.

CONCAWE. 1996. Gas oils (diesel fuels/heating oils). Product dossier no. 95/107. Brussels, Belgium.

IARC. See International Agency for Research on Cancer.

International Agency for Research on Cancer. 1989. Diesel fuels. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans 45:219. http://193.51.164.11/htdocs/monographs/vol45/45-05.htm

NPS. See U.S. National Park Service.

Total Petroleum Hydrocarbon Criteria Working Group. 1997. Volume III: Selection of representative TPH fractions based on fate and transport considerations Amherst Scientific Publishers. Amherst, MA. http://www.aehs.com/publications/catalog/contents/Volume3.pdf

Total Petroleum Hydrocarbon Criteria Working Group. 1998. Volume I: Analysis of petroleum hydrocarbons in environmental media. Amherst Scientific Publishers. Amherst, MA. http://www.aehs.com/publications/catalog/contents/Volume1.pdf

TPHCWG. See Total Petroleum Hydrocarbon Criteria Working Group.

U.S. National Park Service. 1997. Environmental contaminants encyclopedia: Diesel oil entry. Water Resources Division, Water Operations Branch. Fort Collins, CO. http://www1.nature.nps.gov/toxic/search/

WHO. See World Health Organization.

World Health Organization. 1996. Environmental health criteria 171: Diesel fuel and exhaust emissions. Geneva. http://www.inchem.org/documents/ehc/ehc/ehc171.htm

Chevron Products Co. 2001. Material safety data sheet 6894: Chevron LS diesel 2. San Ramon, CA.

ECOTOXICITY:
A series of studies on the acute toxicity of 4 diesel fuel samples were conducted by one laboratory using water accommodated fractions. The range of effective (EC50) or lethal concentrations (LC50) expressed as loading rates were: The 96-hour LC50 for rainbow trout (Salmo gairdneri) is 21-210 mg/l. The 48-hour EC50 for daphnia (Daphnia magna) is 20-210 mg/l. The 72-hour EC50 in alga (Raphidocellus subcapitata) is 2.6-25 mg/l.
ENVIRONMENTAL FATE:
On release to the environment the lighter components of diesel fuel will generally evaporate but depending on local environmental conditions (temperature, wind, mixing or wave action, soil type, etc.) the remainder may become dispersed in the water column or absorbed to soil or sediment. Diesel fuel would not be expected to be "readily biodegradable". In a modified Strum test (OECD method 301B) approximately 40% biodegradation was recorded over 28 days. However, it has been shown that most hydrocarbon components of diesel fuel are degraded in soil in the presence of oxygen. Under anaerobic conditions, such as in anoxic sediments, rates of biodegradation are negligible.

CONCAWE. 1996. Gas oils (diesel fuels/heating oils). Product dossier no. 95/107. Brussels, Belgium.

The dossier summarizes the physical and chemical properties and toxicological, health, safety and environmental information available on gas oils, these include diesel fuels and heating oils.

International Agency for Research on Cancer. 1989. Diesel fuels. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans 45:219.

Overall evaluation:
Marine diesel fuel is possibly carcinogenic to humans (Group 2B).
Distillate (light) diesel fuels are not classifiable as to their carcinogenicity to humans (Group 3).

Total Petroleum Hydrocarbon Criteria Working Group. 1998. Volume I: Analysis of petroleum hydrocarbons in environmental media. Amherst Scientific Publishers. Amherst, MA.

DIESEL FUEL

Transportation diesels are manufactured primarily from distilled fractions of crude oil with some blending with cracked gas oils. The major components of diesels are similar to those present in the crude oil, but include a higher fraction of aromatics (up to 30 to 40%). Diesel fuel is essentially the same as furnace oil, but the proportion of cracked gas oil is usually less than in furnace oil. Although cracking processes also produce small alkenes as well as aromatics, the small alkenes are not in the diesel carbon range and end up in the gasoline pool. The typical carbon range for diesel #1 grades is C8 to C17 range, with the majority in the C10 to C14 range (similar to Jet A and kerosene). The typical carbon range for diesel # 2 fuels is C8 to C26 , with the majority in the C10 to C20 range (similar to fuel oil No. 2). In all cases, the majority of the fuels is 60-90% normal, branched, and cyclic alkanes.

Total Petroleum Hydrocarbon Criteria Working Group. 1997. Volume III: Selection of representative TPH fractions based on fate and transport considerations Amherst Scientific Publishers. Amherst, MA.

> For the EC >12 to 16 aliphatic fraction of petroleum hydrocarbons, the representative water solubility is 0.00076 mg/L, and the log K_{oc} is 6.7 (K_{oc} = 5,011,872).

World Health Organization. 1996. Environmental health criteria 171: Diesel fuel and exhaust emissions. Geneva.

Draws on findings from over 600 studies to evaluate the risks to human health and the environment posed by exposure to diesel fuel and diesel exhaust emissions. The two categories of exposure are evaluated in separate parts.

The evaluation of diesel fuel opens with a discussion of the complexity of these mixtures and the many variables that affect their quality and composition. An evaluation of toxicity studies in laboratory animals and in vitro test systems concludes that diesel fuel has low acute toxicity when administered via oral, dermal, and inhalation routes. Findings on embryotoxicity, teratogenicity, mutagenicity, and genotoxicity were judged to be either negative or equivocal. In view of inadequacies in the few studies of carcinogenic risks, the report concludes that the main effect of exposure on human health is dermatitis following skin contact.

The second and largest part evaluates diesel exhaust emissions. A review of the abundant data demonstrating adverse effects on the environment concludes that the major components of diesel exhaust contribute to acid deposition, tropospheric ozone formation, and global warming. The most extensive sections discuss the epidemiological studies in humans and studies in experimental animals considered useful for the assessment of risks to human health. Although a number of epidemiological studies have indicated an increased risk of lung cancer in bus and railroad workers, all studies suffered from weaknesses. The report concludes that diesel exhaust is probably carcinogenic to humans, and that inhalation of diesel exhaust contributes to both neoplastic and non-neoplastic diseases, including asthma. The report further concludes that the particulate phase has the greatest effect on human health.

Gasoline, CAS # 8006-61-9

Data Point	Data Summary	Reference
Water solubility	Insoluble	ATSDR 1995
K_{oc}	Log K_{oc} = 1.81 to 4.56 (K_{oc} = 65 to 36,300)	ATSDR 1995
Soil half-life		
BCF		
Ingestion toxicity	No NOAEL identified. Lowest LOAELs for endpoints relevant to human toxicity (body weight, gastrointestinal effects) were 2,000 mg/kg in 28-day studies in rats. The oral LD_{50} in rats was 14,063 mg/kg	ATSDR 1995
Carcinogenicity	No studies were located regarding cancer in humans or animals after oral exposure to gasoline. Gasoline is possibly carcinogenic to humans (Group 2B) by inhalation exposure.	ATSDR 1995 IARC 1989
Fish toxicity	96-hour LC_{50} in rainbow trout is 2.7 mg/l (based on values for BTEX).	Chevron 2001
Aq. invert. tox	48-hour LC_{50} in Daphnia magna is 3.0 mg/L (based on values for BTEX).	Chevron 2001
Aq. amph. tox		

Agency for Toxic Substances and Disease Registry. 1995. Toxicological profile for automotive gasoline. Atlanta, GA. http://www.atsdr.cdc.gov/toxprofiles/tp72.html

ATSDR. See Agency for Toxic Substances and Disease Registry.

Chevron Products Company. 2001. MSDS 2655: Regular unleaded gasoline. San Ramon, CA.

IARC. See International Agency for Research on Cancer.

International Agency for Research on Cancer. 1989. Gasoline. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans 45:159. http://193.51.164.11/htdocs/monographs/vol45/45-03.htm

Agency for Toxic Substances and Disease Registry. 1995. Toxicological profile for gasoline. Atlanta, GA.

Report summarized by ATSDR in the form of ToxFAQs document; relevant sections follow:

ToxFAQs™ for Automotive Gasoline, CAS# 8006-61-9, September 1996

"SUMMARY: Exposure to automotive gasoline most likely occurs from breathing its vapor at a service station while filling a car's fuel tank. At high levels, automotive gasoline is irritating to the lungs when breathed in and irritating to the lining of the stomach when swallowed. Exposure to high levels may also cause harmful effects to the nervous system.

Typically, gasoline contains more than 150 chemicals, including small amounts of benzene, toluene, xylene, and sometimes lead. How the gasoline is made determines which chemicals are present in the gasoline mixture and how much of each is present. The actual composition varies with the source of the crude petroleum, the manufacturer, and the time of year.

What happens to automotive gasoline when it enters the environment? Small amounts of the chemicals present in gasoline evaporate into the air when you fill the gas tank in your car or when gasoline is accidentally spilled onto surfaces and soils or into surface waters. Other chemicals in gasoline dissolve in water after spills to surface waters or underground storage tank leaks into the groundwater. In surface releases, most chemicals in gasoline will probably evaporate; others may dissolve and be carried away by water; a few will probably stick to soil. The chemicals that evaporate are broken down by sunlight and other chemicals in the air. The chemicals that dissolve in water also break down quickly by natural processes.

Many of the harmful effects seen after exposure to gasoline are due to the individual chemicals in the gasoline mixture, such as benzene and lead. Inhaling or swallowing large amounts of gasoline can cause death. Inhaling high concentrations of gasoline is irritating to the lungs when breathed in and irritating to the lining of the stomach when swallowed. Gasoline is also a skin irritant. Breathing in high levels of gasoline for short periods or swallowing large amounts of gasoline may also cause harmful effects on the nervous system. Serious nervous system effects include coma and the inability to breathe, while less serious effects include dizziness and headaches. There is not enough information available to determine if gasoline causes birth defects or affects reproduction. The Department of Health and Human Services (DHHS) and the International Agency for Research on Cancer (IARC) have not classified automotive gasoline for carcinogenicity. Automotive gasoline is currently undergoing review by the EPA for cancer classification. Some laboratory animals that breathed high concentrations of unleaded gasoline vapors continuously for 2 years developed liver and kidney tumors. However, there is no evidence that exposure to gasoline causes cancer in humans.

Chevron Products Company. 2001. MSDS 2655: Regular unleaded gasoline. San Ramon, CA.

ECOTOXICITY:
Gasoline studies have been conducted in the laboratory under a variety of test conditions with a range of fish and invertebrate species. An even more extensive database is available on the aquatic toxicity of individual aromatic constituents. The majority of published studies do not identify the type of gasoline evaluated, or even provide distinguishing characteristics such as aromatic content or presence of lead alkyls. As a result, comparison of results among studies using open and closed vessels, different ages and species of test animals and different gasoline types, is difficult.

The bulk of the available literature on gasoline relates to the environmental impact of monoaromatic (BTEX) and diaromatic (naphthalene, methylnaphthalenes) constituents. In general, non-oxygenated gasoline exhibits some short-term toxicity to freshwater and marine organisms, especially under closed vessel or flow-through exposure conditions in the laboratory. The components which are the most prominent in the water soluble fraction and cause aquatic toxicity, are also highly volatile and can be readily biodegraded by microorganisms.

The 96-hour LC50 in rainbow trout (Oncorhynchus mykiss) is 2.7 mg/l (BTEX). The 48-hour LC50 in daphnia (Daphnia magna) is 3.0 mg/l (BTEX). The 96-hour LC50 in sheepshead minnow (Cyprinodon variegatus) is 8.3 mg/l (BTEX). The 96-hour LC50 in mysid shrimp (Mysidopsis bahia) is 1.8 mg/l (BTEX).

International Agency for Research on Cancer. 1989. Gasoline. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans 45:159.

In reference to inhalation exposure to gasoline, IARC concluded the following:

- There is inadequate evidence for the carcinogenicity in humans of gasoline.
- There is limited evidence for the carcinogenicity in experimental animals of unleaded automotive gasoline.
- Gasoline is possibly carcinogenic to humans (Group 2B).

Iron Oxide, CAS # 1309-37-1

Data Point	Data Summary	Reference
Water solubility	Insoluble.	HSDB 2002
K_{oc}	No data.	
Soil half-life	Stable.	
BCF	No data.	
Ingestion toxicity	Iron oxide is regulated by the FDA for use as a food coloring and in food packaging; it is generally recognized as safe. Severe toxicity may result in children following ingestion of more than 0.5 g of iron. In adults, chronic excessive ingestion may lead to toxicity, manifested by hemosiderosis, disturbances in liver function, diabetes mellitus, and possible endocrine disturbances and cardiovascular effects. EPA has established a secondary drinking water regulation of 0.3 mg/L for iron, based on aesthetic endpoints. Intraperitoneal LD_{50} is 5,400 mg/kg in mice.	21 CFR 73.200, 186.1300, and 186.1374 (Amdur et al. 1991) EPA 1992 DHHS 1987
Carcinogenicity	Not classifiable as to its carcinogenicity in humans.	IARC 1987
Fish toxicity Aq. invert. tox Aq. amph. tox	EPA set an ambient water quality criteria level of 1 mg/L for protection of aquatic life from iron, equivalent to 2.9 mg Fe_2O_3/L.	EPA 1999

Amdur, M.O., J. Doull, and C.D. Klaassen (eds.). 1991 *Casarett and Doull's Toxicology: The Basic Science of Poisons.* 4th edition. Pergamon Press, Inc. Elmsford, NY.

DHHS. See U.S. Department of Health and Human Services.

EPA. See U.S. Environmental Protection Agency.

Hazardous Substances Databank. 2002. On-line database. National Library of Medicine. Bethesda, MD. http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB

HSDB. See Hazardous Substances Databank.

IARC. See International Agency for Research on Cancer.

International Agency for Research on Cancer. 1987. Haematite and ferric oxide. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Supplement 7:216. http://193.51.164.11/htdocs/monographs/suppl7/haematite.html

U.S. Department of Health and Human Services (DHHS). 1987. Registry of Toxic Effects of Chemical Substances (RTECS). DHHS NIOSH Publication No. 87-114. U.S. Government Printing Office. Washington, DC.

U.S. Environmental Protection Agency. 1992. Secondary drinking water regulations: Guidance for nuisance chemicals. EPA 810/K-92-001. Office of Water. Washington, DC.

U.S. Environmental Protection Agency. 1999. National recommended water quality criteria--Correction. EPA 822-A-99-01. Office of Water. Washington, DC.

Amdur, M.O., J. Doull, and C.D. Klaassen (eds.). 1991 *Casarett and Doull's Toxicology: The Basic Science of Poisons.* 4th edition. Pergamon Press, Inc. Elmsford, NY.

> Acute iron toxicity is nearly always due to accidental ingestion of iron-containing medicines, and most often occurs in children. ... Severe toxicity occurs after ingestion of more than 0.5 g of iron or 2.5 g of ferrous sulfate. ... Chronic toxicity or iron overload in adults is a more common problem. ... The pathologic consequences of iron overload are similar regardless of basic cause. The body iron content is increased to between 20 and 40 g. Most of the extra iron is hemosiderin. Greatest concentrations are in parenchymal cells of liver and pancreas, as well as endocrine organs and heart. ... Further clinical effects may include disturbances in liver function, diabetes mellitus, and even endocrine disturbances and cardiovascular effects.

Hazardous Substances Databank. 2002. On-line database. National Library of Medicine. Bethesda, MD.

HSDB is a toxicology data file on the National Library of Medicine's (NLM) Toxicology Data Network (TOXNET®). It focuses on the toxicology of potentially hazardous chemicals. It is enhanced with information on human exposure, industrial hygiene, emergency handling procedures, environmental fate, regulatory requirements, and related areas. All data are referenced and derived from a core set of books, government documents, technical reports and selected primary journal literature. HSDB is peer-reviewed by the Scientific Review Panel (SRP), a committee of experts in the major subject areas within the data bank's scope. HSDB is organized into individual chemical records, and contains over 4500 such records.

The following are the human health and environmental fate summaries from HSDB:

Human Health Effects:

Evidence for Carcinogenicity:

Classification of carcinogenicity: 1) evidence in humans: inadequate; 2) evidence suggesting lack of carcinogenicity in animals. Overall summary evaluation of carcinogenic risk to humans is Group 3: The agent is not classifiable as to its carcinogenicity to humans. /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. S7 216 (1987)]**PEER REVIEWED**

A4; Not classifiable as a human carcinogen. /Iron oxide dust and fume (Fe2O3), as Fe/
[American Conference of Governmental Industrial Hygienists. TLVs & BEIs: Threshold limit Values for Chemical Substances and Physical Agents andBiological Exposure Indices for 2002. Cincinnati, OH. 2002. 37]**QC REVIEWED**

Human Toxicity Excerpts:

HEMATITE DUST CAUSES A BENIGN PNEUMOCONIOSIS ... .
[The Merck Index. 9th ed. Rahway, New Jersey: Merck & Co., Inc., 1976. 525]**PEER REVIEWED**

IT IS CLEAR ... THAT UNDER CONDITIONS OF HEAVY EXPOSURE TO HEMATITE DUST, PULMONARY CLEARANCE MECHANISMS MAY BE OVERWHELMED. ... UPPER LOBES & UPPER PARTS OF LOWER LOBES TEND TO BE MORE AFFECTED BY FIBROSIS THAN LOWER PARTS OF LOWER LOBES. ALSO, PERIPHERIES OF LUNGS TEND TO BE MORE AFFECTED THAN CENTRAL REGIONS.
[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. V1 32]**PEER REVIEWED**

... 1 CASE OF BRONCHIAL CARCINOMA & 1 GROSS PULMONARY TUBERCULOSIS /WERE REPORTED/ AMONG GROUP OF HEMATITE MINERS.
[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. V1 32]**PEER REVIEWED**

... EXCESSIVE INCIDENCE OF BRONCHIAL CANCER /WAS REPORTED/ AMONG IRON-ORE MINERS OF LORRAINE BASIN. ... 64 CASES OF DISEASE /WERE REPORTED/

AMONG 10000 ... MINERS ... COMPARED WITH 28 CASES AMONG 10000 WORKERS FROM IRON WORKS IN SAME DISTRICT. CO-EXISTENCE OF LUNG CANCER & SILICOSIS ... NOTED IN 10 EX-MINERS ON PENSION.
[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. V1 33]**PEER REVIEWED**

OCCLUSIVE & OBLITERATIVE VASCULAR CHANGES IN HEMATITE LUNG ARE REALLY THOSE OF SILICOSIS. ONLY FEATURE PECULIAR TO HEMATITE LUNG IS INTENSE ACCUM OF IRON-DUST IN & AROUND PULMONARY BLOOD VESSELS.
[HEATH D ET AL; BR J DIS CHEST 72 (2): 88-94 (1978)]**PEER REVIEWED**

LUNG FUNCTION TESTS IN 14 WORKERS EXPOSED ON AVG OF 10 YR TO PURE IRON OXIDE DUST SEEMS TO SUPPORT OPINION THAT PURE IRON OXIDE IS NOT FIBROGENIC IN LUNG.
[TECULESCU D, ALBU A; INT ARCH ARBEITSMED 31 (2): 163-70 (1973)]**PEER REVIEWED**

Eight of 25 welders exposed chiefly to iron oxide for an average of 18.7 (range 3 to 32) years had reticulonodular shadows on chest x-rays consistent with siderosis but no reduction in pulmonary function; exposure levels ranged from 0.65 to 47 mg/cu m. In another study, 16 welders with an average exposure of 17.1 (range 7 to 30) years also had x-rays suggesting siderosis and spirograms which were normal; however, the static and functional compliance of the lungs was reduced; some of the welders were smokers. The welders with the lowest compliance complained of dyspnea.
[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**

... Some electric arc welders exposed mainly to iron oxide fume showed generalized discrete densities in their chest X-ray films. None of these welders, however, showed any demonstrable clinical disability.
[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. 803]**PEER REVIEWED**

... Workers exposed to iron oxide fume and silica amy develop a "mixed dust pneumoconiosis."
[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. 803]**PEER REVIEWED**

... Little or no physical disability was associated with the presence of iron oxide fume and dust in the lungs ... The deposition and collection of iron oxide in the lung ... has been termed "siderosis". ... Siderosis is considered a benign condition and does not progress to fibrosis. Six to 10 years of exposure to iron oxide fume is generally required in order to produce siderosis. Little or no clinical changes are found upon physical examination of workers diagnosed with siderosis.
[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. 803]**PEER REVIEWED**

Studies in foundry workers exposed to iron oxide have shown an increase in lung cancer incidence among these 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. 804]**PEER REVIEWED**

... Three cases of severe pulmonary changes related to iron oxide exposure from welding fumes /was reported/. The three men in this study suffered from cough and shortness of breath, X-ray examination revealed diffuse fibrosis.
[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. 286]**PEER REVIEWED**

... The lung function of 16 welders exposed to iron oxide fumes /was compared/ with 13 non-exposed men of similar age, height and smoking habits. Static and functional lung compliance of exposed men was found to be significantly different from that of controls. Silica was stated to be absent in ... /the/ study.
[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. 287]**PEER REVIEWED**

HIGHER CONCN OF SILICA & IRON ... FOUND IN LUNGS OF HEMATITE MINERS WITH FIBROSIS (ASSOC OR NOT WITH PULMONARY TUBERCULOSIS) OR ... BRONCHIAL CARCINOMA THAN IN ... THOSE WITH NO SUCH PATHOLOGY ... LEVELS IN THOSE WITH CARCINOMA WERE NOT HIGHER THAN ... IN THOSE WITH FIBBROSIS (ACCOMPANIED OR NOT BY TUBERCULOSIS) BUT NO CARCINOMA ... .
[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. V1 32]**PEER REVIEWED**

ON BASIS OF EPIDEMIOLOGICAL EVIDENCE, EXPOSURE TO HEMATITE DUST MAY BE REGARDED AS INCR RISK OF LUNG CANCER DEVELOPMENT IN MAN. RISK IS MANIFEST IN UNDERGROUND WORKERS BUT NOT SURFACE WORKERS ... NOT KNOWN WHETHER EXCESS RISK IS DUE TO RADIOACTIVITY IN AIR OF MINES, INHALATION OF FERRIC OXIDE OR SILICA, OR COMBINATION ... .
[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. V1 36]**PEER REVIEWED**

MOST COMPREHENSIVE EPIDEMIOLOGICAL STUDY...DEATH CERTIFICATES /WERE STUDIED/ OF 5811 MALE RESIDENTS OF HEMATITE MINING REGION OF CUMBERLAND, ENG WHO DIED BETWEEN 1948 & 1967. ... 36 LUNG CANCER DEATHS AMONG UNDERGROUND HEMATITE WORKERS AS COMPARED WITH CA 21 EXPECTED ON BASIS OF EITHER LOCAL NON-MINER DEATHS OR NATIONAL AVG.
[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. V1 33]**PEER REVIEWED**

/IN STUDY OF 5811 HEMATITE WORKERS' DEATH CERTIFICATES IN CUMBERLAND, ENG/ NO EXCESS MORTALITY FROM LUNG CANCER WAS FOUND AMONG SURFACE IRON-ORE MINERS, & FOR IRON MINERS IN GENERAL MORTALITY FROM CANCERS OF SITES OTHER THAN LUNG WAS CLOSE TO NATIONAL AVG.
[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. V1 33]**PEER REVIEWED**

... STUDY OF IRON-ORE MINERS IN LORRAINE BASIN OF FRANCE, COMPARED INCIDENCE OF BRONCHOGENIC CARCINOMA IN 1095 IRON-ORE MINERS & 940 NON-MINERS (ALL MALES ...): 3.3% INCIDENCE IN FORMER IS SIGNIFICANTLY HIGHER (P= 0.01) THAN IN LATTER (1.5%). ... USE OF TOBACCO IS COMMON AMONG THEIR IRON WORKERS.

[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. V1 33]**PEER REVIEWED**

10 MG/CU M FOR IRON OXIDE FUME IS SUGGESTED TO PREVENT DEVELOPMENT OF X-RAY CHANGES IN LUNGS ON LONG-TERM EXPOSURE. ... MORE INFORMATION IS ALSO NEEDED ON RELATIONSHIP OF IRON DEPOSITS IN LUNGS TO CONCOMITANT EXPOSURE TO OTHER INDUSTRIAL DUSTS.
[American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values for Substances in Workroom Air. Third Edition, 1971. Cincinnati, Ohio: AmericanConference of Governmental Industrial Hygienists, 1971. (Plus supplements to 1979) 136]**PEER REVIEWED**

Medical Surveillance:

/Protect/ from exposure those individuals with pulmonary diseases.
[ITII. Toxic and Hazardous Industrial Chemicals Safety Manual. Tokyo, Japan: The International Technical Information Institute, 1988. 284]**PEER REVIEWED**

The following medical procedures should be made available to each employee who is exposed to iron oxide fume at potentially hazardous levels: ... A complete history and physical examination ... Examination of the respiratory system should be stressed; 14" X 17" chest roentgenogram; ... FVC and FEV (1 sec). ... The aforementioned medical examinations should be repeated on an annual basis, except that an x-ray is considered necessary only when indicated by the results of pulmonary function testing.
[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**

Populations at Special Risk:

... Individuals with pulmonary diseases.
[ITII. Toxic and Hazardous Industrial Chemicals Safety Manual. Tokyo, Japan: The International Technical Information Institute, 1988. 284]**PEER REVIEWED**

Probable Routes of Human Exposure:

... FOLLOWING OCCUPATIONS ... /ENTAIL/ RISK OF INHALATION OF DUST & FUMES OF IRON & ITS VARIOUS ALLOYS & CMPD: IRON-ORE MINERS; ARC WELDERS; GRINDERS: POLISHERS; SILVER FINISHERS; METAL WORKERS. ... /ALSO/ BOILER MAKERS ... .
[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. V1 30]**PEER REVIEWED**

Environmental Fate & Exposure:

Natural Pollution Sources:

Alpha-form occurs in nature as the mineral hematite; gamma-form occurs as the mineral maghemite
[Budavari, S. (ed.). The Merck Index - Encyclopedia of Chemicals, Drugs and Biologicals. Rahway, NJ: Merck and Co., Inc., 1989. 632]**PEER REVIEWED**

International Agency for Research on Cancer. 1987. Haematite and ferric oxide. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Supplement 7:216.

Overall evaluation
Ferric oxide is *not classifiable as to its carcinogenicity to humans (Group 3)*.
Haematite is *not classifiable as to its carcinogenicity to humans (Group 3)*.
Underground haematite mining with exposure to radon is *carcinogenic to humans (Group 1)*.

U.S. Environmental Protection Agency. 1992. Secondary drinking water regulations: Guidance for nuisance chemicals. EPA 810/K-92-001. Office of Water. Washington, DC.

The U.S. Environmental Protection Agency (EPA) has established National Primary Drinking Water Regulations that set mandatory water quality standards for drinking water contaminants. These are enforceable standards called "maximum contaminant levels" or "MCLs", which are established to protect the public against consumption of drinking water contaminants that present a risk to human health. An MCL is the maximum allowable amount of a contaminant in drinking water which is delivered to the consumer .

In addition, EPA has established National Secondary Drinking Water Regulations that set non-mandatory water quality standards for 15 contaminants. EPA does not enforce these "secondary maximum contaminant levels" or "SMCLs." They are established only as guidelines to assist public water systems in managing their drinking water for aesthetic considerations, such as taste, color and odor. These contaminants are not considered to present a risk to human health at the SMCL.

Table I. Secondary Maximum Contaminant Levels

Contaminant	**Secondary MCL**	**Noticeable Effects above the Secondary MCL**
Aluminum	0.05 to 0.2 mg/L*	colored water
Chloride	250 mg/L	salty taste
Color	15 color units	visible tint
Copper	1.0 mg/L	metallic taste; blue-green staining
Corrosivity	Non-corrosive	metallic taste; corroded pipes/ fixtures staining
Fluoride	2.0 mg/L	tooth discoloration
Foaming agents	0.5 mg/L	frothy, cloudy; bitter taste; odor
Iron	0.3 mg/L	rusty color; sediment; metallic taste; reddish or orange staining
Manganese	0.05 mg/L	black to brown color; black staining; bitter metallic taste
Odor	3 TON (threshold odor number)	"rotten-egg", musty or chemical smell
pH	6.5 - 8.5	*low pH:* bitter metallic taste; corrosion *high pH:* slippery feel; soda taste; deposits
Silver	0.1 mg/L	skin discoloration; graying of the white part of the eye
Sulfate	250 mg/L	salty taste
Total Dissolved Solids (TDS)	500 mg/L	hardness; deposits; colored water; staining; salty taste
Zinc	5 mg/L	metallic taste
** mg/L is milligrams of substance per liter of water*		

U.S. Environmental Protection Agency. 1999. National recommended water quality criteria--Correction. EPA 822-A-99-01. Office of Water. Washington, DC.

SUMMARY: EPA is publishing a compilation of its national recommended water quality criteria for 157 pollutants, developed pursuant to section 304(a) of the Clean Water Act (CWA or the Act). These recommended criteria provide guidance for States and Tribes in adopting water quality standards under section 303(c) of the CWA. Such standards are used in implementing a number of environmental programs, including setting discharge limits in National Pollutant Discharge Elimination System (NPDES) permits. These water quality criteria are not regulations, and do not impose legally binding requirements on EPA, States, Tribes or the public.

Lead, CAS #7439-92-1

Data Point	Data Summary	Reference
Water solubility	Insoluble.	ATSDR 1999
K_{oc}	Most lead is retained strongly in soil, and very little is transported into surface water or groundwater. Lead is strongly sorbed to organic matter in soil, and although not subject to leaching, it may enter surface waters as a result of erosion of lead-containing soil particulates.	ATSDR 1999
Soil half-life	Stable.	
BCF	Median BCF = 42 in fish.	Eisler 1988
Ingestion toxicity	EPA's reference dose workgroup concluded it was inappropriate to develop a reference dose, or an acceptable daily intake, for lead because some of lead's adverse effects, particularly changes in the levels of certain blood enzymes and in aspects of children's neurobehavioral development, may occur at blood lead levels so low as to be essentially without a threshold. A lowest lethal dose of 1,400 mg/kg was estimated for lead oxide in dogs, equivalent to 1,307 mg/kg lead.	EPA 1993 ATSDR 1999
Carcinogenicity	Lead is a probable human carcinogen, but a quantitative estimate of risk is not appropriate given current data.	EPA 1993
Avian toxicity	5-day dietary LC_{50} in Japanese quail >5,000 ppm in food, equivalent to approximately 875 mg/kg.	HSDB 2002
Fish toxicity	96-hour LC_{50} in rainbow trout is 1.17 mg/L.	EPA 2002
Aq. invert. tox	48-hour LC_{50} in *Daphnia magna* is 4.4 mg/L.	EPA 2002
Aq. amph. tox	The 30-day LC_{50} value for *Rana pipiens* was 105 mg/L.	Eisler 1988

Agency for Toxic Substances and Disease Registry. 1999. Toxicological profile for lead Atlanta, GA. http://www.atsdr.cdc.gov/toxprofiles/tp13.html

ATSDR. See Agency for Toxic Substances and Disease Registry.

Eisler, R. 1988. Lead hazards to fish, wildlife and invertebrates: A synoptic review. Patuxent Wildlife Research Center, U.S. Fish and Wildlife Service. Laurel, MD. http://www.pwrc.usgs.gov/new/chrback.htm

EPA. See U.S. Environmental Protection Agency.

U.S. Environmental Protection Agency. 1993. Integrated risk information system. Office of Research and Development. Cincinnati, OH. http://www.epa.gov/iris/subst/0277.htm

U.S. Environmental Protection Agency. 2002. Ecotox database: Lead. Mid-Continent Ecology Division, National Health and Environmental Effects Research Laboratory, Office of Research and Development. Duluth, MN. http://www.epa.gov/ecotox/

Agency for Toxic Substances and Disease Registry. 1999. Toxicological profile for lead. Atlanta, GA.

Report summarized by ATSDR in the form of ToxFAQs document; relevant sections follow:

HIGHLIGHTS: Exposure to lead can happen from breathing workplace air or dust, eating contaminated foods, or drinking contaminated water. Children can be exposed from eating lead-based paint chips or playing in contaminated soil. Lead can damage the nervous system, kidneys, and reproductive system.

What happens to lead when it enters the environment? Lead itself does not break down, but lead compounds are changed by sunlight, air, and water. When lead is released to the air, it may travel long distances before settling to the ground. Once lead falls onto soil, it usually sticks to soil particles. Movement of lead from soil into groundwater will depend on the type of lead compound and the characteristics of the soil. Much of the lead in inner-city soils comes from old houses painted with lead-based paint.

How can lead affect my health?
Lead can affect almost every organ and system in your body. The most sensitive is the central nervous system, particularly in children. Lead also damages kidneys and the reproductive system. The effects are the same whether it is breathed or swallowed. At high levels, lead may decrease reaction time, cause weakness in fingers, wrists, or ankles, and possibly affect the memory. Lead may cause anemia, a disorder of the blood. It can also damage the male reproductive system. The connection between these effects and exposure to low levels of lead is uncertain. The Department of Health and Human Services has determined that lead acetate and lead phosphate may reasonably be anticipated to be carcinogens based on studies in animals.
There is inadequate evidence to clearly determine lead's carcinogenicity in people. Small children can be exposed by eating lead-based paint chips, chewing on objects painted with lead-based paint, or swallowing house dust or soil that contains lead. Children are more vulnerable to lead poisoning than adults. A child who swallows large amounts of lead may develop blood anemia, severe stomachache, muscle weakness, and brain damage. A large amount of lead might get into a child's body if the child ate small pieces of old paint that contained large amounts of lead. If a child swallows smaller amounts of lead, much less severe effects on blood and brain function may occur. Even at much lower levels of exposure, lead can affect a child's mental and physical growth. Exposure to lead is more dangerous for young and unborn children. Unborn children can be exposed to lead through their mothers. Harmful effects include premature births, smaller babies, decreased mental ability in the infant, learning difficulties, and reduced growth in young children. These effects are more common if the mother or baby was exposed to high levels of lead.

Eisler, R. 1988. Lead hazards to fish, wildlife and invertebrates: A synoptic review. Patuxent Wildlife Research Center, U.S. Fish and Wildlife Service. Laurel, MD.

SUMMARY

Lead (Pb) and its compounds have been known to man for about 7,000 years, and Pb poisoning has been recognized for at least 2,500 years. All credible evidence indicates that Pb is neither essential nor beneficial to living organisms, and that all measured effects are adverse--including those on survival, growth, reproduction, development, behavior, learning, and metabolism.

Various living resources are at increased risk from Pb: migratory waterfowl that frequent hunted areas and ingest shot; avian predators that eat game wounded by hunters; domestic livestock near smelters, refineries, and Pb battery recycling plants; captive zoo animals and domestic livestock held in enclosures coated with Pb-based paints; wildlife that forage extensively near heavily traveled roads; aquatic life in proximity to mining activities, areas where Pb arsenate pesticides are used, metal finishing industries, organolead industries, and areas of Pb aerosol fallout; and crops and invertebrates growing or living in Pb-contaminated soils.

Adverse effects on aquatic biota reported at waterborne Pb concentrations of 1.0 to 5.1 ug/l included reduced survival, impaired reproduction, reduced growth, and high bioconcentration from the medium. Among sensitive species of birds, survival was reduced at doses of 50 to 75 mg Pb2+/kg body weight (BW) or 28 mg organolead/kg BW, reproduction was impaired at dietary levels of 50 mg Pb /kg, and signs of poisoning were evident at doses as low as 2.8 mg organolead/kg BW. In general, forms of Pb other than shot (or ingestible Pb objects), or routes of administration other than ingestion, are unlikely to cause clinical signs of Pb poisoning in birds. Data for toxic and sublethal effects of Pb on mammalian wildlife are missing. For sensitive species of domestic and laboratory animals, survival was reduced at acute oral Pb doses of 5 mg/kg BW (rat), at chronic oral doses of 5 mg/kg BW (dog), and at dietary levels of 1.7 mg/kg BW (horse). Sublethal effects were documented in monkeys exposed to doses as low as 0.1 mg Pb/kg BW daily (impaired learning at 2 years postadministration) or fed diets containing 0.5 mg Pb/kg (abnormal social behavior). Signs of Pb exposure were recorded in rabbits given 0.005 mg Pb/kg BW and in mice given 0.05 mg Pb/kg BW. Tissue Pb levels were elevated in mice given doses of 0.03 mg Pb/kg BW, and in sheep given 0.05 mg Pb/kg BW. In general, organolead compounds were more toxic than inorganic Pb compounds, food chain biomagnification of Pb vas negligible, and younger organisms were most susceptible. More research seems merited on organolead toxicokinetics (including effects on behavior and learning), and on mammalian wildlife sensitivity to Pb and its compounds.

Recent legislation limiting the content of Pb in paints, reducing the Pb content in gasoline, and eliminating the use of Pb shot nationwide (Pb shot phaseout program/schedule starting in 1986, and fully implemented by 1991) in waterfowl hunting areas will substantially reduce environmental burdens of Pb and may directly benefit sensitive fishery and wildlife resources. Continued nationwide monitoring of Pb in living resources is necessary in order to correlate reduced emission sources with reduced tissue Pb concentrations.

U.S. Environmental Protection Agency. 1993. Integrated risk information system. Office of Research and Development. Cincinnati, OH.

STATUS OF DATA FOR Lead and compounds (inorganic)
File First On-Line 03/01/1988

Category (section)	**Status**	**Last Revised**
Oral RfD Assessment (I.A.)	message	02/01/1991
Inhalation RfC Assessment (I.B.)	no data	
Carcinogenicity Assessment (II.)	on-line	11/01/1993

_I.A. Reference Dose for Chronic Oral Exposure (RfD)
Substance Name -- Lead and compounds (inorganic)
CASRN -- 7439-92-1

A great deal of information on the health effects of lead has been obtained through decades of medical observation and scientific research. This information has been assessed in the development of air and water quality criteria by the Agency's Office of Health and Environmental Assessment (OHEA) in support of regulatory decision-making by the Office of Air Quality Planning and Standards (OAQPS) and by the Office of Drinking Water (ODW). By comparison to most other environmental toxicants, the degree of uncertainty about the health effects of lead is quite low. It appears that some of these effects, particularly changes in the levels of certain blood enzymes and in aspects of children's neurobehavioral development, may occur at blood lead levels so low as to be essentially without a threshold. The Agency's RfD Work Group discussed inorganic lead (and lead compounds) at two meetings (07/08/1985 and 07/22/1985) and considered it inappropriate to develop an RfD for inorganic lead. For additional information, interested parties are referred to the 1986 Air Quality Criteria for Lead (EPA-600/8-83/028a-dF) and its 1990 Supplement (EPA/600/8-89/049F).

II.A. Evidence for Human Carcinogenicity
__II.A.1. Weight-of-Evidence Characterization
Classification -- B2; probable human carcinogen
Basis -- Sufficient animal evidence. Ten rat bioassays and one mouse assay have shown statistically significant increases in renal tumors with dietary and subcutaneous exposure to several soluble lead salts. Animal assays provide reproducible results in several laboratories, in multiple rat strains with some evidence of multiple tumor sites. Short term studies show that lead affects gene expression. Human evidence is inadequate.

_II.B. Quantitative Estimate of Carcinogenic Risk from Oral Exposure
Not available.
Quantifying lead's cancer risk involves many uncertainties, some of which may be unique to lead. Age, health, nutritional state, body burden, and exposure duration influence the absorption, release, and excretion of lead. In addition, current knowledge of lead pharmacokinetics indicates that an estimate derived by standard procedures would not truly describe the potential risk. Thus, the Carcinogen Assessment Group recommends that a numerical estimate not be used.

U.S. Environmental Protection Agency. 2002. Ecotox database: Lead. Mid-Continent Ecology Division, National Health and Environmental Effects Research Laboratory, Office of Research and Development. Duluth, MN.

The ECOTOXicology database is a source for locating single chemical toxicity data for aquatic life, terrestrial plants and wildlife. ECOTOX integrates three toxicology effects databases: AQUIRE (aquatic life), PHYTOTOX (terrestrial plants), and TERRETOX (terrestrial wildlife). These databases were created by the U.S. EPA, Office of Research and Development (ORD), and the National Health and Environmental Effects Research Laboratory (NHEERL), Mid-Continent Ecology Division.

Scientific name, Common name	End-point	Effect	Trend --------- Effect %	Media Type	Duration ---------- Exp Typ	Conc (ug/L)	Signif ------- Level	Response Site ------- BCF	Ref #
									Test Loc: LAB
CAS #/Chemical: 7439921, Lead									
Daphnia magna Water flea	LC50	MOR	INC --------	FW	48 H ---------- S	T 4400, 3600 - 5300		------	11181
Oncorhynchus mykiss Rainbow trout, donaldson trout	LC50	MOR	INC --------	FW	96 H ---------- F	T 1.17 mg/L		------	14367

Manganese Dioxide, CAS #1313-13-9 (MnO_2)

Data Point	Data Summary	Reference
Water solubility	Insoluble.	ATSDR 2000
K_{oc}	Sorption of manganese is complicated by redox reactions that produce compounds of different oxidation states. Under aerobic conditions, insoluble manganese 3+ and 4+ compounds predominately form.	HSDB 2002
Soil half-life	Insoluble manganese 3+ and 4+ compounds in sediments may be reduced by manganese-reducing bacteria to soluble manganese 2+ compounds.	HSDB 2002
BCF	A BCF of 100 to 600 was estimated for fish.	ATSDR 2000
Ingestion toxicity	The mean manganese intake in the United States from foodstuffs for a 2-year-old child is estimated to be about 1.5 mg/child/day. The mean manganese intake in the United States from foodstuffs for 25- to 30-year-old man and woman are estimated to be about 2.1 and 2.7 mg/person/day, respectively. ATSDR adopted the National Research Council's upper range of the estimated safe and adequate daily dietary intake of 5 mg/day as a provisional guidance value for oral exposure to manganese; this is equivalent to 0.07 mg/kg/day. EPA has set an oral reference dose of 0.14 mg/kg/day for manganese intake. An oral LD_{50} of 11,250 mg/kg was identified for manganese in rats, equivalent to 17,803 mg MnO_2/kg.	HSDB 2002 ATSDR 2000 EPA 1996 ATSDR 2000
Carcinogenicity	Not classifiable as to carcinogenicity in humans.	EPA 1996
Fish toxicity	96-hour LC_{50} for manganese in rainbow trout was 4.83 mg/L, equivalent to 7.64 mg MnO_2/L.	Reimer 1988
Aq. invert. tox	48-hour LC_{50} for manganese in *Daphnia magna* was 4.7 to 56.1 mg/L, equivalent to 7.4 to 89 mg MnO_2/L.	Reimer 1988
Aq. amph. tox	No data.	

Agency for Toxic Substances and Disease Registry. 2000. Toxicological profile for manganese. Atlanta, GA. http://www.atsdr.cdc.gov/toxprofiles/tp151.html

ATSDR. See Agency for Toxic Substances and Disease Registry.

EPA. See U.S. Environmental Protection Agency.

Hazardous Substances Databank. 2002. On-line database. National Library of Medicine. Bethesda, MD. http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB

HSDB. See Hazardous Substances Databank.

Reimer, P. 1988. Environmental effects of manganese and proposed freshwater guidelines to protect aquatic life in British Columbia. Department of Chemical and Bio-Resource Engineering. University of British Columbia.

U.S. Environmental Protection Agency. 1996. Integrated risk information system. Office of Research and Development. Cincinnati, OH. http://www.epa.gov/iris/subst/0373.htm

Agency for Toxic Substances and Disease Registry. 2000. Toxicological profile for manganese. Atlanta, GA.

Report summarized by ATSDR in the form of ToxFAQs document; relevant sections follow:

Manganese is an essential trace element and is necessary for good health. Manganese can be found in several food items, including grains and cereals, and is found in high amounts in other foods, such as tea.

What happens to manganese when it enters the environment? Manganese can enter the air from iron, steel, and power plants, coke ovens, and from dust from mining operations. It can enter the water and soil from natural deposits, disposal of wastes, or deposits from airborne sources. Manganese exists naturally in rivers, lakes, and underground water. Plants in the water can take up some of the manganese from water and concentrate it.

How can manganese affect my health? Some individuals exposed to very high levels of manganese for long periods of time in their work developed mental and emotional disturbances and slow and clumsy body movements. This combination of symptoms is a disease called "manganism." Workers usually do not develop symptoms of manganism unless they have been exposed to manganese for many months or years. Manganism occurs because too much manganese injures a part of the brain that helps control body movements. Exposure to high levels of airborne manganese, such as in a manganese foundry or battery plant, can affect motor skills such as holding one's hand steady, performing fast hand movements, and maintaining balance. Exposure to high levels of the metal may also cause respiratory problems and sexual dysfunction. There are no human cancer data available for manganese. Exposure to high levels of manganese in food resulted in a slightly increased incidence of pancreatic tumors in male rats and thyroid tumors in male and female mice. The EPA has determined that manganese is not classifiable as to human carcinogenicity.

Daily intake of small amounts of manganese is needed for growth and good health in children. Manganese is constantly present in the mother and is available to the developing fetus during pregnancy. Manganese is also transferred from a nursing mother to her infant in breast milk at levels that are appropriate for proper development. Children, as well as adults, who lose the ability to remove excess manganese from their bodies develop nervous system problems. Because at certain ages children take in more than adults, there is concern that children may be more susceptible to the toxic effects of excess manganese. Animal studies indicate that exposure to high levels of manganese can cause birth defects in the unborn. There is no information on whether mothers exposed to excess levels of manganese can transfer the excess to their developing fetus during pregnancy or to their nursing infant in breast milk.

The EPA has set a non-enforceable guideline for the level of manganese in drinking water at 0.05 milligrams per liter (0.05 mg/L). The National Research Council has recommended safe and adequate daily intake levels for manganese that range from 0.3 to 1 mg/day for children up to 1 year, 1 to 2 mg/day for children up to age 10, and 2 to 5 mg/day for children 10 and older.

Hazardous Substances Databank. 2002. On-line database. National Library of Medicine. Bethesda, MD.

HSDB is a toxicology data file on the National Library of Medicine's (NLM) Toxicology Data Network (TOXNET®). It focuses on the toxicology of potentially hazardous chemicals. It is enhanced with information on human exposure, industrial hygiene, emergency handling procedures, environmental fate, regulatory requirements, and related areas. All data are referenced and derived from a core set of books, government documents, technical reports and selected primary journal literature. HSDB is peer-reviewed by the Scientific Review Panel (SRP), a committee of experts in the major subject areas within the data bank's scope. HSDB is organized into individual chemical records, and contains over 4500 such records.

The following is the HSDB summary of human health and environmental fate information:

HUMAN HEALTH EFFECTS:

HUMAN TOXICITY EXCERPTS:

DIVALENT MANGANESE(2+) IS ABOUT 2.5 TO 3 TIMES MORE TOXIC THAN IS MANGANESE(3+) ... THE ANION OF A MANGANESE SALT INFLUENCES THE OVERALL MANGANESE TOXICITY. INHALATION OF MANGANESE CMPD IN AEROSOLS OR FINE DUSTS PRODUCES "METAL FUME FEVER". /MANGANESE AND MANGANESE SALTS/ [Venugopal, B. and T.D. Luckey. Metal Toxicity in Mammals, 2. New York: Plenum Press, 1978. 265]**PEER REVIEWED**

THE USUAL FORM OF CHRONIC MANGANESE POISONING PRIMARILY INVOLVES CNS. EARLY SYMPTOMS INCL LANGUOR, SLEEPINESS, & WEAKNESS IN LEGS. A STOLID MASKLIKE APPEARANCE OF FACE, EMOTIONAL DISTURBANCES SUCH AS UNCONTROLLABLE LAUGHTER, & SPASTIC GAIT WITH TENDENCY TO FALL IN WALKING ARE FINDINGS IN MORE ADVANCED CASES. [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. 354]**PEER REVIEWED**

ONSET /OF CHRONIC POISONING/ IS INSIDIOUS, WITH APATHY, ANOREXIA, & ASTHENIA. MANGANESE PSYCHOSIS ... HAS CERTAIN DEFINITIVE FEATURES: UNACCOUNTABLE LAUGHTER, EUPHORIA, IMPULSIVENESS, & INSOMNIA, FOLLOWED BY OVERPOWERING SOMNOLENCE. HEADACHE ... LEG CRAMPS; SEXUAL EXCITEMENT, FOLLOWED BY IMPOTENCE /ARE OFTEN PRESENT/. [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. 1762]**PEER REVIEWED**

FOLLOWING OR CONCOMITANTLY WITH ... /MANIFESTATIONS OF MANGANESE PSYCHOSIS/ ARE SPEECH DISTURBANCES WITH SLOW & DIFFICULT ARTICULATION, INCOHERENCE, EVEN COMPLETE MUTENESS. MASK-LIKE FACIES SETS IN ... WITH GENERAL CLUMSINESS OF MOVEMENT, NOTICEABLE IN ALTERED GAIT & BALANCE ... . [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. 1762]**PEER REVIEWED**

ABSOLUTE DETACHMENT, BROKEN BY SPORADIC & SPASMODIC LAUGHTER, ENSUES & AS IN EXTRAPYRAMIDAL AFFECTIONS, SALIVATION & EXCESSIVE SWEATING

OCCUR. DESPITE SEVERE INCAPACITATIONS ... PT SURVIVES, ALTHOUGH PERMANENTLY DISABLED UNLESS TREATED; CHRONIC MANGANESE POISONING IS NOT A FATAL DISEASE. [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. 1762]**PEER REVIEWED**

STEVEDORES REGULARLY EMPLOYED IN HANDLING MANGANESE ORES DEVELOPED PNEUMONIA FROM WHICH 31% DIED, & ... /CASES OF/ PNEUMONIA IN NORWEGIAN WORKERS FOLLOWING INTRODUCTION OF AN ELECTRIC FURNACE FOR MANGANESE ORE, /&/ ... PNEUMONIAS FROM DRILLING & BLASTING IN UNDERGROUND MOROCCAN MINES ... /ARE REPORTED/. [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. 1762]**PEER REVIEWED**

... /MANGANESE PSYCHOSIS/ IS NOTABLY ABSENT FROM REPORTS OF MANGANESE POISONING IN STEEL FOUNDRIES & ORE-CRUSHING PLANTS IN UNITED STATES. /MANGANESE/ [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. 1755]**PEER REVIEWED**

THERE IS CURRENTLY NO EVIDENCE THAT HUMAN EXPOSURE TO MANGANESE AT LEVELS
COMMONLY OBSERVED IN AMBIENT ATMOSPHERE RESULTS IN ADVERSE HEALTH EFFECTS.
ONLY ... HEALTH EFFECTS ATTRIBUTABLE TO MANGANESE IN AMBIENT AIR WERE FOUND IN PERSONS LIVING IN IMMEDIATE VICINITY OF 2 MAJOR POINT SOURCES IN NORWAY & ITALY. [National Research Council. Drinking Water & Health Volume 1. Washington, DC: National Academy Press, 1977. 268]**PEER REVIEWED**

... /THE HOMEOSTATIC SYSTEM/ REGULATING MECHANISM, PLUS TENDENCY FOR EXTREMELY LARGE DOSE OF MANGANESE SALTS TO CAUSE GI IRRITATION, ACCOUNTS FOR LACK OF SYSTEMIC TOXICITY FOLLOWING ORAL ADMIN OR DERMAL APPLICATION. [Doull, J., C.D. Klaassen, and M. D. Amdur (eds.). Casarett and Doull's Toxicology. 2nd ed. New York: Macmillan Publishing Co., 1980. 450]**PEER REVIEWED**

... MANGANESE TOXICITY IN MAN ARISING FROM EXCESSIVE INTAKES IN FOODS & BEVERAGES HAS NEVER BEEN REPORTED & IS DIFFICULT TO VISUALIZE EVER ARISING, EXCEPT WHERE INDUSTRIAL CONTAMINATION OCCURS. [National Research Council. Drinking Water and Health. Volume 3. Washington, DC: National Academy Press, 1980. 336]**PEER REVIEWED**

... WHILE HIGH LEVELS OF MANGANESE MAY INCREASE ANEMIA BY INTERFERING WITH IRON ABSORPTION, IRON DEFICIENCY MAY INCREASE AN INDIVIDUAL'S SUSCEPTIBILITY TO MANGANESE POISONING. [National Research Council. Drinking Water and Health. Volume 3. Washington, DC: National Academy Press, 1980. 336]**PEER REVIEWED**

MOST CONSPICUOUS INVOLVEMENT OF EYES IS IN DECR MOVEMENT OF EYELIDS & EYES. IT IS SAID, HOWEVER, THAT NEITHER PARESIS OF EYE MUSCLES NOR NYSTAGMUS OCCURS, & THAT MANGANESE POISONING DIFFERS FROM POSTENCEPHALITIC PARKINSONISM IN HAVING NO ACCOMPANYING OCULOGYRIC CRISIS OR LOSS OF BELL'S PHENOMENON. [Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986. 575]**PEER REVIEWED**

CHRONIC MANGANESE TOXICITY ... FOLLOWING CHRONIC EXPOSURE TO MANGANESE THROUGH INHALATION ... FOR PERIODS OF FROM 6 MO TO 2 YR RESULTS IN "MANGANISM", A DISEASE OF CNS INVOLVING PSYCHIC & NEUROLOGICAL DISORDERS. ... /IT/ IS REVERSIBLE IF RECOGNIZED EARLY & ... EXPOSURE ... ELIMINATED. [Venugopal, B. and T.D. Luckey. Metal Toxicity in Mammals, 2. New York: Plenum Press, 1978. 267]**PEER REVIEWED**

... Marked differences in individual susceptibility to inhaled manganese ... may have been caused by alcoholism, syphilis, carbon monoxide, lesions of the excretory system, or the physiological or pathological condition of the respiratory tract. ... [USEPA; Health Assessment Document: Manganese p.9-5 (1984) EPA-600/8-83-013F]**PEER REVIEWED**

Individual susceptibility to the adverse effects of manganese varies considerably. The minimum dose that produces effects on the central nervous system is not known and, with few exceptions, such effects have been observed only in occupationally exposed individuals. Only one epidemiological report is available on adverse effects from drinking water contaminated with manganese. Sixteen cases of manganese poisoning, three of which were fatal (including one suicide), in a small Japanese community, have been described. About 400 dry cell batteries were found buried within 2 m of a well used as a water supply. The manganese content of the water was about 14 mg/l and concentrations of about 8 and 11 mg/l were found in two other wells. The subjects exhibited psychological and neurological disorders associated with manganese poisoning, and high manganese and zinc levels were found in organs at autopsy. [WHO; Environ Health Criteria: Manganese-Executive Summary p.4 (1981)]**PEER REVIEWED**

Acute systemic intoxication rarely occurs after oral administration. ... Aside from parenteral routes, systemic poisoning may result from chronic inhalation or chronic ingestion; chronic exposure to low concentrations may lead to the accumulation of toxic concentrations in critical organs. The brain appears to sustain permanent cellular damage at exposure levels which do not otherwise affect a person. The characteristic pathological lesion in man is destruction of the ganglion cells of the basal ganglia, although symptoms appear before damage becomes discernible. Symptoms of workers exposed to manganese dusts include masklike facial expression, spastic gait, tremors, slurred speech, sometimes dystonia, fatiguability, anorexia, asthenia, apathy, and inability to concentrate. /Manganese salts/ [Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984.,p. II-144]**PEER REVIEWED**

Manganese poisoning is clinically characterized by the central nervous system involvement including psychiatric symptoms, extrapyramidal signs, and other neurological manifestations. The onset of symptoms is usually insidious and progressive ... . The initial manifestations are usually vague complaints of asthenia, anorexia, apathy, insomnia or drowsiness, and a slowing down in performing motor acts. ... Other frequent symptoms of the early and established phases of the poisoning are malaise, somnolence, imbalance while walking or on arising, slurred speech, difficulty with line movements (handwriting), limb stiffness, diminished libido or impotence. Sometimes, mental languor and lack of energy are prominent symptoms at the onset. Tremor, paresthesia, muscle cramps, memory loss, swallowing difficulty, urinary urgency or incontinence,

lumbosacral pain, metallic taste, anorexia, and nervousness are less frequent ... . /Manganese/ [Chang, L.W. (ed.). Toxicology of Metals. Boca Raton, FL: Lewis Publishers, 1996 416]**PEER REVIEWED**

Psychiatric symptoms are well described in the manganese miners and include sleep disturbance, disorientation, emotional liability, compulsive acts, hallucinations, illusions, and delusions. A marked somnolence is also observed, most often to be replaced later by stubborn insomnia. Most of the cases show emotional incontinence, particularly forced laughing. ... Patients may abruptly burst into laughter or (more rarely) into tears without any apparent reason. Frequent irritability and nervousness resulted in arguments and friction among miners, occasionally approaching violence. /Manganese/ [Chang, L.W. (ed.). Toxicology of Metals. Boca Raton, FL: Lewis Publishers, 1996 416]**PEER REVIEWED**

... A population of Australian aborigines that exhibited signs of motor neuron disease similar, but not identical, to manganism seen among manganese miners /was identified/. These aborigines resided on Groote Eylandt in the Gulf of Carpenteria in northern Australia. Groote Eylandt has unusually rich deposits of manganese ore on or near the surface, and these have been commercially exploited. In a detailed survey of these natives, the authors determined that signs of intoxication were not simply related to potential exposure either in their home life or occupationally. Rather, the appearance of signs and symptoms was the result of a complex interplay of synergistic factors including genetics; inborn errors of trace element metabolism; life styles; dietary deficiencies of dopamine oxidation inhibitors, thiamine, and ascorbic acid; calcium deficiency; and possibly, smoking and excessive alcohol intake. /Manganese/ [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. 2118]**PEER REVIEWED**

The results of a study of 30 workers exposed to manganese in two different steel mills in Sweden have been described in two publications. The exposed group comprised the 15 "most exposed" workers from each plant. These were compared to a control group of 60 workers from a steel mill in which there was no manganese exposure. Exposed workers were matched 1 to 2 with control workers on the basis of age, geographic area of residence, and type of work. The concentration of manganese in the breathing zone of the exposed group was measured at the time of the study, and the mean concentration ranged from 0.19 to 0.45 mg/cu m. Peak exposures as high as 1.62 mg/ml were reported. ... There had been no change in exposure levels for the past 17 or 18 years. The duration of exposure ranged from 1 year to 35 years or more. ... There were no differences between the exposed and control subjects with respect to general health status and medical history or in any of the psychiatric examinations. Two of the neurological examinations, auditory-evoked response and diadochokinesometry, revealed slight differences between exposed and control workers. /Manganese/ [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. 2115]**PEER REVIEWED**

The 132 employees of the same factory were divided into four groups, based on the nature of their job assignments and their probable exposure to manganese. The 17 workers in groups 0 were office workers and probably experienced no exposure to manganese, whereas the 24 men in group 3 and

the 8 men in group 4 were furnace workers in the smelting department. Workers in group 4, which included the six cases of manganese intoxication ... experienced the greatest exposure because they operated electrodes at the furnaces and for about 30 min every day were exposed to airborne concentrations of manganese that were estimated to be as high as 28.8 mg/cu m. Measurements made at the time of the study indicated that workers in exposure group 1 were exposed to average concentrations of manganese in air of 0.1 mg/cu m and those in group 2 to 0.5 to 1.5 mg/cu m. Parkinsonism was not diagnosed in any workers other than the six in group 4. However, some symptoms of neurological impairment (e.g., muscle weakness, muscle cramps, loss of libido) were increased in groups 1 and 2 compared to group 0. Blood samples were collected from all workers; the mean blood concentrations in the four exposure groups were 1.49 + 0.92, 2.52 + 0.86, 3.13 + 1.56, and 14.6 + 15.5 ug/100 ml, showing a clear correlation between the level of exposure and the concentration of manganese in the blood. However, ... no correlation between duration of exposure and concentrations of manganese in the blood and ... blood levels were indicators of current exposure, but not of chronic exposure. /Manganese/ [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. 2115]**PEER REVIEWED**

Clinical examination of the six workers revealed bradykinesia, masklike facial features, clumsiness, impaired dexterity, and abnormal gait. Three of the workers had mild tremor and micrographia. ... Measurement of manganese concentrations in blood, scalp hair, and pubic hair from these workers revealed values that were from 3 to 300 times normal concentrations. /Manganese/ [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. 2114]**PEER REVIEWED**

Studies of neurologic and psychologic symptoms in workers exposed to manganese suggest that exposure to airborne dust below (5 mg/cu m) for 1 year or more may still lead to clinical signs of intoxication, especially respiratory symptoms, changes in lung ventilatory parameters, alteration of neurofunctional performances, & hypercalcemia. /Manganese/ [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. 1587]**PEER REVIEWED**

"Locura manganica" or "manganese madness" is the insidious onset of psychiatric symptoms, including apathy, insomia, confusion, bizarre behavior, visual hallucinations, emotional lability, decr libido, impotence, & anxiety. Neurologic manifestations include nystagmus, disequilibrium, paresthesia, memory impairment, a vocal pattern described as "whispering speech", problems with fine motor movement, lumbosacral pain, urgency, & incontinence. The neurologic syndrome is similar to Parkinson's disease with tremor, ataxia, loss of memory, flat affect, muscle rigidity, & gait disturbances. Unlike Parkinson's, however pathologic lesions are found in the globus pallidus & the striatum rather than the globus pallidus & the substantia nigra. /Manganese/ [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. 1587]**PEER REVIEWED**

The most common respiratory symptom is dyspnea. Because of its low solubility in water, airborne manganese does not cause oral or dermal problems. Instead, it penetrates the lower respiratory tract toward the alveolar membrane, leading to the development of manifestations of pneumonitis, pneumonia, & bronchitis. /Manganese/ [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. 1587]**PEER REVIEWED**

The usual form of chronic manganese poisoning primarily involves the central nervous system (CNS). Early symptoms include languor, sleepiness, and weakness in the legs. A stolid, mask like appearance of the face emotional disturbances such as uncontrollable laughter, and spastic gait with a tendency to fall when walking are findings in more advanced cases. In addition, a high incidence of pneumonia has been found in workers exposed to the dust or fume of some manganese compounds. [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. 876]**PEER REVIEWED**

... Manganese concentrations up to 170 Mg/cu m and averaging 47 Mg/cu m /were reported/ in a mill where 11 of 34 employees were found to suffer from manganese poisoning. No cases occurred among workers exposed at less than 30 Mg/cu m. However, studies in another ore mill with dusty operations, where workers performed similar tasks with more modern equipment and local exhaust ventilation, revealed manganese concentrations averaging 2.3 Mg/cu m (from two air samples), with 6 Mg/cu m at the dustiest operation. [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. 876]**PEER REVIEWED**

... 5 Cases /were described/ showing signs indicative of chronic manganese in a study of 71 employees working in a steel mill in Pennsylvania from 1957 to 1965. Of the three workers exposed to manganese fume, one worked as a pourer and had an average exposure of 13.3 mg/cu m ; a second was a "hot blastman" with an average exposure of 0.33 mg/cu m. The third was a general laborer in the blast furnace area. From the data presented, it can be estimated that the third worker's average exposure was about 0.8 Mg/cu m. The two employees exposed to manganese dust had worked in the plant since 1943. Starting in 1957, they worked in a newly installed crushing and screening unit. In 1958, breathing zone manganese concentrations were estimated to average 35 mg/cu m . Between 1958 and 1966, average dust exposures at the original unit and at one installed in 1962 varied from 0.7 to 30 mg/cu m manganese with a monthly average of about 20 mg/cu m. [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. 877]**PEER REVIEWED**

... 7 cases and 15 borderline cases of manganese /were recorded/ in 75 Pennsylvania plants where 144 workers were found exposed to manganese dust or fume concentrations exceeding 5 Mg/cu m. Of the seven cases, four resulted from exposure to manganese dust and three from manganese fumes. No cases were reported in 48 workers exposed at air concentrations of fume or dust of less than 5 Mg/cu m. Because the only results reported were

based on the criterion in use, i.e., whether or not the exposure of the affected workers exceeded 5 mg/cu m, the study is of little value in pinpointing the relative degree of hazard between manganese fume and dust. /Manganese dust and fume/ [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. 877]**PEER REVIEWED**

In a study on 72 Chilean miners exposed to manganese concn in air of 62.5-250 mg/cu m, 12 (16.5%) were found to have neurological disorders. The avg exposure time was 178 days, with a range of 49-480 days. A further study on 370 miners exposed to manganese concn in air of 0.5-46 mg/cu m showed that 15 workers (4%) had contracted typical manganese intoxication. ... the average time of exposure was 8 years, 2 months, with a range of 9 months- 16 years. [WHO; Environ Health Criteria 17: Manganese p.68 (1981)]**PEER REVIEWED**

16 cases of manganese poisoning /from drinking water/, 3 of which were fatal (including 1 suicide), in a small Japanese community /were studied/. About 400 dry-cell batteries were found buried within 2 m of a well used as a water supply. The manganese content of the water was about 14 mg/liter & concn of 8 & 11 mg/liter were found in two other wells. All 16 intoxicated subjects drank water from these wells. The subjects exhibited psychological & neurological disorders assoc with manganese poisoning, & high manganese & zinc levels were found in organs at autopsy. [WHO; Environ Health Criteria 17: Manganese p.72 (1981)]**PEER REVIEWED**

The primary target organs of managanese toxicity are the brain and the lungs. The toxicity to the brain is manifested as a chronic disorder of the central nervous system resembling Parkinsonism. Toxicity to the lungs is manifested as increased susceptibility to bronchitis or, in more serious cases, manganic pneumonia. [Zenz, C., O.B. Dickerson, E.P. Horvath. Occupational Medicine. 3rd ed. St. Louis, MO., 1994 543]**PEER REVIEWED**

ENVIRONMENTAL FATE/EXPOSURE SUMMARY:

Manganese compounds are found in the earth's crust in the form of numerous minerals such as pyrolusite, romanechite, manganite, hausmannite. Manganese compounds enter the atmosphere and aqueous environment from the weathering of rocks and windblown soil. Manganese compounds and ions may also be released by anthropogenic sources into the environment through their use as antiknock agents (methylcyclopentadienyl manganese tricarbonyl), antiseptics (potassium permanganate), catalysts (manganous acetate), dietary supplements (manganese chloride), dry cells (manganese chloride), feed additives (manganese sulfate, manganese carbonate), fertilizers (manganese sulfate), pesticides (potassium permanganate), and pigments (manganese sulfate). Manganese is multi-valent and can exist in the 2+, 3+, 4+, 6+, and 7+ oxidation states, with 2+, 3+, and 4+ being the dominant oxidation states in the environment. Manganese 2+ is the most stable oxidation state in water while manganese 3+ and 4+ compounds are immobile solids. Organic matter may reduce manganese 3+ and 4+ compounds, resulting in the formation of soluble manganese 2+ compounds. Soluble manganese 2+ compounds do not strongly complex to soil and organic matter. Thus manganese 2+ compounds are relatively mobile and may potentially leach into surface and groundwater. As ions or insoluble solids, most

manganese compounds are not expected to volatilize from water and moist soil surfaces. Manganese compounds, released into the ambient atmosphere are expected to exist in the particulate phase. In the particulate phase, manganese compounds may be removed from the air by wet and dry deposition. Manganese compounds do not bioconcentrate in humans and animals. However, manganese is an essential nutrient for most plants and animals. Dietary intake is the primary source of exposure to manganese compounds for humans. Occupational exposure to elevated levels of manganese compounds may occur through inhalation in the workplace where manganese compounds are produced or used. (SRC) **PEER REVIEWED**

Reimer, P. 1988. Environmental effects of manganese and proposed freshwater guidelines to protect aquatic life in British Columbia. Department of Chemical and Bio-Resource Engineering. University of British Columbia.

Manganese is a naturally occurring substances that is present in surface waters and biota. Aquatic organisms have exhibited toxic responses to manganese in surface waters and regulatory bodies in some jurisdictions have established guidelines for levels of manganese in surface water to protect aquatic life. In British Columbia, a guideline of 0.1 mg/L was established by the Ministry of Environment, Lands and Parks, although it was recognized that the scientific data on which this guideline was based were weak. Toxicity tests applicable to aquatic life in BC waters were commissioned to strengthen the relevant data base and to apply the British Columbia procedures for deriving water quality criteria in an effort to establish more defensible guidelines for the protection of aquatic life in BC. Acute and chronic toxicity tests were conducted on fish, invertebrates and freshwater algae. Acute tests included 48 and 96 hour LC50's, while chronic tests included reproduction, growth and survival endpoints. A range of organisms was chosen in order to evaluate the range of sensitivities to manganese. The possible relationship between water hardness and toxicity to manganese was also investigated at water hardnesses of 25, 100 and 250 mg/L CaCO3.

Data were also gathered from literature sources in support of the new toxicity information. Both acute and chronic studies were identified for fish species resident in BC fresh waters. The collective data were evaluated for suitability with respect to the BC water quality guideline derivation process. Toxicity test data that met the requirements for use in guideline derivation were screened for sensitivity in order to fulfill the objective of developing a guideline protective of the most sensitive aquatic organisms.

A pattern emerged whereby the concentrations of manganese at which adverse effects were observed increased with increasing water hardness. This pattern was identified in both the literature data and in all but one of the new toxicity tests commissioned by the Ministry of Environment, Lands and Parks. Acute and chronic regression equations were developed using the most sensitive data for various (in both cases six) water hardness values. The acute equation was $Y = 0.0441X + 1.81$ and the chronic equation was $Y = 0.0176 + 2.42$, where X = water hardness in mg/L CaCO3 and Y = Mn concentration in mg/L. The equations were used to predict manganese concentrations at water hardness increments of 25 mg/L CaCO3 over the hardness range of 25-325 mg/L CaCO3, a range that encompasses the vast majority of BC surface waters. A factor of safety of 0.25 was applied to the predicted concentrations to account for uncertainty and was based on scientific judgement and the strength of the data set used in the derivation process. The resulting acute manganese concentrations ranged from 0.6 to 3.8 mg/L and are proposed as guidelines for exposure of less than 96 hours. The resulting chronic manganese concentrations ranged from 0.6 to 1.9 mg/L and are proposed as guidelines for exposure exceeding 96 hours. While BC and other surface water data indicate that manganese rarely exceeds concentrations of 1 mg/L, it is recognized that natural events may result in periodic increases. The application of guidelines intended to protect aquatic life from anthropogenic sources of manganese should reflect this in the sampling methodology requirements.

U.S. Environmental Protection Agency. 1996. Integrated risk information system: Manganese. Office of Research and Development. Cincinnati, OH.

_I.A.1. Oral RfD Summary

Critical Effect	Experimental Doses*	UF	MF	RfD
CNS effects Human Chronic Ingestion Data NRC, 1989; Freeland-Graves et al., 1987; WHO, 1973;	NOAEL (food): 0.14 mg/kg-day LOAEL: None	1	1	1.4E-1 mg/kg-day

*Conversion Factors and Assumptions -- The NOAEL of 10 mg/day (0.14 mg/kg-day for 70 kg adult) for chronic human consumption of manganese in the diet is based on a composite of data from several studies.

II.A. Evidence for Human Carcinogenicity

__II.A.1. Weight-of-Evidence Characterization

Classification -- D; not classifiable as to human carcinogenicity

Basis -- Existing studies are inadequate to assess the carcinogenicity of manganese.

__II.A.2. Human Carcinogenicity Data

None.

__II.A.3. Animal Carcinogenicity Data

Inadequate.

MTBE, CAS #1634-04-4 (methyl *tert*-butyl ether)

Data Point	Data Summary	Reference
Water solubility	48,000 mg/L	ATSDR 1996
K_{oc}	Log K_{oc} estimated as 1.05 and calculated as 2.89 (K_{oc}s = 11.2 and 776, respectively) Log K_{oc}s reported as 1.091, 1.035, 1.049 (K_{oc}s = 12.3,10.8, and 11.2, respectively)	ATSDR 1996 Malcolm Pirnie 1999
Soil half-life	Rapid volatilization from surface soils, little degradation in subsurface.	ATSDR 1996
BCF	Insignificant (BCF = 1.5 to 3, with levels rapidly declining after exposure ends). Log BCF was 0.18 in Japanese carp (BCF = 1.5).	ATSDR 1996 EFDB 2002
Ingestion toxicity	ATSDR derived an intermediate-duration minimal risk level of 0.3 mg/kg/day. An oral rat LD_{50} of 4.0 mL/kg was identified; this is equal to 2,962 mg/kg.	ATSDR 1996 HSDB 2002
Carcinogenicity	Possible human carcinogen at high doses. Cancer slope factor = 0.004 per mg/kg/day.	EPA 1997
Fish toxicity	Rainbow trout LC_{50} is 880 to 1,240 mg/L	Johnson 1998
Aq. invert. tox	*Ceriodaphnia dubia* LC_{50} is 340 to 680 mg/L	Johnson 1998
Aq. amph. tox	100 mg/L led to increased weight, stimulated metamorphosis; <2,000 mg/L had no lethal effect on European common frog tadpoles	Pauli et al. 2000

Agency for Toxic Substances and Disease Registry. 1996. Toxicological profile for methyl *tert*-butyl ether. Atlanta, GA. http://www.atsdr.cdc.gov/toxprofiles/tp91.html

ATSDR. See Agency for Toxic Substances and Disease Registry.

EFDB. See Environmental Fate Database.

Environmental Fate Database. 2002. On-line database. Syracuse Research Corporation. http://esc.syrres.com/efdb.htm

EPA. See U.S. Environmental Protection Agency.

Hazardous Substances Databank. 2002. On-line database. National Library of Medicine. Bethesda, MD. http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB

HSDB. See Hazardous Substances Databank.

Johnson, M.L. 1998. Ecological risk of MTBE in surface waters. John Muir Institute of the Environment, University of California. Davis, CA.

Malcolm Pirnie, Inc. 1999. Technical memorandum: Evaluation of fate and transport of methyl tertiary butyl ether (MTBE) in gasoline following a small spill. Prepared for Oxygenated Fuels Association, Inc. Oakland, CA.

Pauli, B.D., J.A. Perrault, and S.L. Money. 2000. RATL: A database of reptile and amphibian toxicology literature. Technical Report Series No. 357. Canadian Wildlife Service, Headquarters, Hull, Québec, Canada. http://www.cws-scf.ec.gc.ca/nwrc/ratl/about_e.htm

U.S. Environmental Protection Agency. 1997. Drinking water advisory: Consumer acceptability advice and health effects analysis on methyl tertiary-butyl ether (MtBE). EPA-822-F-97-009. Office of Water. Washington, DC.

Agency for Toxic Substances and Disease Registry. 1996. Toxicological profile for methyl *tert*-butyl ether. Atlanta, GA.

Report summarized by ATSDR in the form of ToxFAQs document; relevant sections follow:

ToxFAQs™ for Methyl *tert*-Butyl Ether, CAS# 1634-04-4, September 1997

What happens to methyl tert-butyl ether (MTBE) when it enters the environment? MTBE quickly evaporates from open containers and surface water, so it is commonly found as a vapor in the air. Small amounts of MTBE may dissolve in water and get into underground water. It remains in underground water for a long time. MTBE may stick to particles in water, which will cause it to eventually settle to the bottom sediment. MTBE may be broken down quickly in the air by sunlight. MTBE does not build up significantly in plants and animals.

How can methyl tert-butyl ether (MTBE) affect my health? Breathing small amounts of MTBE for short periods may cause nose and throat irritation. Some people exposed to MTBE while pumping gasoline, driving their cars, or working in gas stations have reported having headaches, nausea, dizziness, and mental confusion. However, the actual levels of exposure in these cases are unknown. In addition, these symptoms may have been caused by exposure to other chemicals. There are no data on the effects in people of drinking MTBE. Studies with rats and mice suggest that drinking MTBE may cause gastrointestinal irritation, liver and kidney damage, and nervous system effects. There is no evidence that MTBE causes cancer in humans. One study with rats found that breathing high levels of MTBE for long periods may cause kidney cancer. Another study with mice found that breathing high levels of MTBE for long periods may cause liver cancer. The Department of Health and Human Services (DHHS), the International Agency for Research on Cancer (IARC), and the EPA have not classified MTBE as to its carcinogenicity.

Has the federal government made recommendations to protect human health? The EPA has issued guidelines recommending that, to protect children, drinking water levels of MTBE not exceed 4 milligrams per liter of water (4 mg/L) for an exposure of 1-10 days, and 3 mg/L for longer-term exposures. The American Conference of Governmental Industrial Hygienists (ACGIH) has recommended an exposure limit of 40 parts of MTBE per million parts of air (40 ppm) for an 8-hour workday, 40-hour workweek.

Environmental Fate Database. 2002. On-line database. Syracuse Research Corporation. http://esc.syrres.com/efdb.htm

CHEMFATE search results: Methyl tert-butyl ether.

BIOC METHYL TERT-BUTYL ETHER CAS# 1634-04-4
Log Bioc. Fact.: 0.18
Species Name : JAPANESE CARP
Remarks : SRC SUGGESTED VALUE
Abbrev. Ref. : FUJIWARA,Y ET AL. (1984)

Hazardous Substances Databank. 2002. On-line database. National Library of Medicine. Bethesda, MD.

HSDB is a toxicology data file on the National Library of Medicine's (NLM) Toxicology Data Network (TOXNET®). It focuses on the toxicology of potentially hazardous chemicals. It is enhanced with information on human exposure, industrial hygiene, emergency handling procedures, environmental fate, regulatory requirements, and related areas. All data are referenced and derived from a core set of books, government documents, technical reports and selected primary journal literature. HSDB is peer-reviewed by the Scientific Review Panel (SRP), a committee of experts in the major subject areas within the data bank's scope. HSDB is organized into individual chemical records, and contains over 4500 such records.

The following is the HSDB summary of human health and environmental fate information:

HUMAN HEALTH EFFECTS:

EVIDENCE FOR CARCINOGENICITY:
A3. A3= Animal 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. 47]**QC REVIEWED**

Evaluation: There is limited evidence in humans for the carcinogenicity of methyl tert-butyl ether. There is limited evidence in experimental animals for the carcinogenicity of methyl tert-butyl ether. Overall evaluation: Methyl tert-butyl ether is not classifiable as to it 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. 73 375 (1999)]**QC REVIEWED**

HUMAN TOXICITY EXCERPTS:
A case of acute renal failure is reported in one of 8 patients (aged 37-75 yr) with a history of biliary colic and radiolucent gallstones who were given continuous methyl tert-butyl ether (MTBE I) infusion through a catheter, 5-10 ml for 7 hr. Hemolysis due to extravasation of MTBE after leakage alongside the catheter was suspected as the cause of the renal failure. Dialysis over 18 days was required before renal function recovered completely. [Ponchon T et al; Lancet 2 (July 30): 276-277 (1988)]**PEER REVIEWED**

PROBABLE ROUTES OF HUMAN EXPOSURE:
NIOSH (NOES Survey 1981-1983) has statistically estimated that 3,522 workers (971 of these are female) are potentially exposed to methyl t-butyl ether in the US(1). Occupational exposure to methyl t-butyl ether may occur during its production or subsequent use, particularly in gasoline, via inhalation or dermal contact. The general population may be exposed to methyl t-butyl ether via inhalation of ambient air especially during refueling operations and from ingestion of ambient and drinking water(SRC). [(1) NIOSH; National Occupational Exposure Survey (NOES) (1983)]**PEER REVIEWED**

Methyl t-butyl ether arithmetic mean concentrations (ug/cu m) in air were

1,500 for manufacturing workers, 5,000 for blending workers, 14,000 transportation workers, 2,600 for distribution workers, 5,200 for gasoline station workers, 660 for mechanics, 61 for professional drivers, 61 for commuters, 30 for other drivers, 390 for gasoline station customers, 4 for manufacturing and blending neighbors, 66 for gasoline station neighbors, and 2.6 for the general public(1). Time-weighted personal-breathing-zone samples among mechanics who repaired motor vehicles ranged from less than 108 ug/cu m to 43,464 ug/cu m(2). A methyl t-butyl ether concentration of 412 ug/cu m was detected in a breathing zone grab sample collected during refueling; ambient air grab samples collected at 2 and 16 minutes post refueling contained methyl t-butyl ether at concentrations of 16.8 and 23.4 ug/cu m, respectively(3). Exposure of Finnish tanker drivers to methyl t-butyl ether during loading and delivery was between 13 and 91 mg/cu m(4). Mean exposure of service station attendants to methyl t-butyl ether was 0.3 ppm (range 0.04 to 3.88 ppm) in 41 personal breathing zone air samples collected in the Phoenix, AZ area and 0.14 ppm (range 0.02 to 0.73 ppm) in 48 personal breathing zone air samples collected in the Los Angeles, CA area(5). [(1) Brown SL; Regul Toxicol Pharmacol. 25: 256-76 (1997) (2) White MC et al; An Investigation of Exposure to Methyl Tertiary Butyl Ether Among Motorists and Exposed Workers in Stamford, Connecticut. USEPA-600-R95-134. Proc Conf MTBE and Other Oxygenates, 1993 D42-D64 (1995) (3) Lindstrom AB, Pleil JD; J Air Waste Manage Assoc 46: 676-82 (1996) (4) Hakkola M, Saarinen L; Ann Occup Hyg 40: 1-10 (1996) (5) Hartle R; Environ Health Perspect 101 (Supp 6): 23-6 (1994)]**PEER REVIEWED**

Occupational exposure to methyl t-butyl ether via short-term exposure, less than 30 minutes (TWA, between 6 and 9 hours) was 11.0 (0.24) ppm for transporting neat methyl t-butyl ether, 5.1 (0.58) ppm for blending neat methyl t-butyl ether, 4.7 (0.77) ppm for service station attendants, 3.3 (0.13) ppm for transporting a methyl t-butyl ether/fuel mix, 1.0 (0.14) ppm for manufacturing-maintenance, 0.85 (0.13) ppm for distributing methyl t-butyl ether, 0.84 (0.06) ppm for manufacturing-routine, and 0.58 (0.10) ppm for blending a methyl t-butyl ether/fuel mix(1). Long-term (93 to 570 minutes) methyl t-butyl ether exposure concentrations for refueling attendants were 0.5 ppm or less; winter and summer geometric mean exposures were 0.2 ppm and 0.08 ppm, respectively(2). Winter and summer mechanic geometric mean exposures to methyl t-butyl ether were 0.12 ppm and 0.03 ppm, respectively; only four individual methyl t-butyl ether samples exceeded 0.5 ppm, these four samples (0.63, 0.86, 1.3, and 2.6 ppm) were taken during shift where mechanics duties included fuel line servicing(2). Short-term (8 to 35 minutes) methyl t-butyl ether exposure for refueling attendants was less than 0.21 ppm, with winter and summer geometric mean exposures of 0.6 and 0.31 ppm, respectively(2). Individual mechanic short-term methyl t-butyl ether exposures were less than 0.91 ppm, with winter and summer geometric mean exposures of 1.04 and 0.42 ppm, respectively(2). [(1) American Petroleum Institute; Petroleum Industry Data Characterizing Occupational Exposures to Methyl Tertiary Butyl Ether (MTBE) 1983-1993. Washington,DC: Amer Petrol Instit, API Publ Noo 4622. Order No. I46220 (1995) (2) American Petroleum Institute; Service Station Personnel Exposures to Oxygenated Fuel Components - 1994. Washington,DC: Amer Petrol Instit, API Publ No 4625 . Oder No I46250 (1995)]**PEER REVIEWED**

ENVIRONMENTAL FATE/EXPOSURE SUMMARY:

Methyl t-butyl ether's production and use as an octane booster in gasoline and in the manufacture of isobutene may result in its release to the

environment through various waste streams. If released to air, a vapor pressure of 250 mm Hg at 25 deg C indicates methyl t-butyl ether will exist solely as a vapor in the ambient atmosphere. Vapor-phase methyl t-butyl ether will be degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals and nitrate radicals; half-lives for these reactions in air are estimated to be 5.5 and 50 days, respectively. Direct photolysis is not expected to be an important removal process since aliphatic ethers do not absorb light in the environmental spectrum. If released to soil, methyl t-butyl ether is expected to have very high mobility based upon a Koc of 6 calculated from a soil/water partition coefficient of 0.0925. Volatilization from moist soil surfaces is expected to be an important fate process based upon a Henry's Law constant of 5.87X10-4 atm-cu m/mole. Methyl t-butyl ether may potentially volatilize from dry soil surfaces based upon its vapor pressure. If released into water, methyl t-butyl ether is not expected to adsorb to suspended solids and sediment in the water column based upon the Koc. 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 4.1 hours and 4.1 days, respectively. A BCF of 1.5 in Japanese carp suggests bioconcentration in aquatic organisms is low. Methyl t-butyl ether is not expected to undergo hydrolysis in the environment due to the lack of hydrolyzable functional groups. In general, most studies have indicated that methyl t-butyl ether is difficult to biodegrade. t-Butyl alcohol was identified as a metabolite of methyl t-butyl ether in a study using an enrichment culture capable of degrading methyl t-butyl ether. Occupational exposure to methyl t-butyl ether may occur during its production or subsequent use, particularly in gasoline, via inhalation or dermal contact. The general population may be exposed to methyl t-butyl ether via inhalation of ambient air especially during refueling operations and from ingestion of ambient and drinking water. (SRC) **PEER REVIEWED**

Johnson, M.L. 1998. Ecological risk of MTBE in surface waters. John Muir Institute of the Environment, University of California. Davis, CA.

Conclusions

- MTBE is present in California's surface waters and aquatic organisms are exposed.
- There is little toxicity of MTBE to aquatic organisms, with the most sensitive taxonomic group tested being green algae.
- One experimental study indicates that fish accumulate MTBE to about 1.5 times the concentration of MTBE in the water column.
- The most conservative toxicity reference value calculated for rainbow trout is 7,000ppb.
- The most conservative hazard quotients for rainbow trout exposed to MTBE in two selected surface waters range from 1 x 10 -3 to 6 x 10 -3 , well below the level that indicates potential adverse ecological effects.
- Adverse effects on rainbow trout are not expected until concentrations of MTBE in the water column reach 4,600 ppb to 4,700 ppb. These levels are much greater than the human health standards for MTBE in drinking water supplies.

Malcolm Pirnie, Inc. 1999. Technical memorandum: Evaluation of fate and transport of methyl tertiary butyl ether (MTBE) in gasoline following a small spill. Prepared for Oxygenated Fuels Association, Inc. Oakland, CA.

Recently it has been suggested that small discrete spills of gasoline containing the fuel oxygenate, MTBE onto the ground surface will result in significant groundwater contamination from MTBE. The purpose of this screening level analysis is to determine whether several hypothetical small spill scenarios, defined as spills less than 4 gallons of gasoline, could result in substantial groundwater contamination by MTBE in comparison to the known contamination caused by releases of gasoline from underground storage tanks. For this analysis, we have divided a small gasoline spill into four stages: 1) spill occurrence; 2) surface evaporation; 3) infiltration; and 4) vadose zone transport to the water table. The literature devoted to analyzing the evaporation of individual gasoline components during the time between the initial spill (Stage 1) and the introduction to groundwater (Stage 4) is extensive. Specifically, researchers have concluded that in most situations, more than 99% of volatile gasoline components will evaporate within a few hours of the spill prior to transport through the vadose zone.

In this analysis, we show that under conservative geologic scenarios, approximately 0.2% of the initial mass of MTBE in a 4 gallon spill on concrete and approximately 0.7% of the initial mass of MTBE in a 1 gallon spill on soil will reach groundwater. Using a conservative mixing cell calculation, we show that this mass of MTBE entering groundwater will result in maximum concentrations of less than 11 ug/l within the immediate vicinity of the spill. For spills less than 1 gallon, we show that negligible amounts of MTBE are expected to reach the groundwater. Based on these highly conservative gasoline spill scenarios, MTBE impacts to groundwater from small spills will be significantly smaller than impacts caused by releases from leaking underground storage tanks (e.g., 200 ug/l). Thus, small spills are not expected to represent a significant source of groundwater contamination relative to other sources of MTBE groundwater contamination. Nonetheless, in limited circumstances, small spills will impact shallow aquifers, and thus, warrant the support of outreach programs on proper handling of gasoline, and instruction of the public on appropriate procedures to minimize the occurrence of small gasoline spills.

Pauli, B.D., J.A. Perrault, and S.L. Money. 2000. RATL: A database of reptile and amphibian toxicology literature. Technical Report Series No. 357. Canadian Wildlife Service, Headquarters, Hull, Québec, Canada.

The RATL (Reptile and Amphibian Toxicology Literature) database contains data extracted from the primary literature for amphibian and reptile ecotoxicology studies published up to and including 1997; there are some data from studies published in 1998 and 1999. As of September, 2000, there was approximately 2000 references in the database. Citations were gathered through searches of various literature databases, but these searches concentrated on the environmental pollution literature with the result that the bibliography cannot be considered exhaustive.

U.S. Environmental Protection Agency. 1997. Drinking water advisory: Consumer acceptability advice and health effects analysis on methyl tertiary-butyl ether (MtBE). EPA-822-F-97-009. Office of Water. Washington, DC.

The EPA Office of Water is issuing this Advisory to provide guidance for communities that may be exposed to drinking water contaminated with MtBE. The Advisory provides an analysis of current health hazard information and an evaluation of currently available data on taste and odor problems associated with MtBE contamination of water, as the latter affect consumer acceptance of the water resource. This Advisory does not recommend either a low-dose oral cancer risk number or a reference dose (RfD) due to certain limitations of available data for quantifying risk. Guidance is given on the concentrations at which taste and odor problems likely would be averted, and how far these are from MtBE concentrations at which toxic effects have been seen in test animals. (The measure used is called a "margin of exposure" or MoE. For instance, if a measured concentration is 100,000 times less than the range of observation of effects in test animals, the margin of exposure is 100,000.

Conclusion and Recommendation

This Advisory recommends that keeping levels of contamination in the range of 20 to 40 µg/L or below to protect consumer acceptance of the water resource would also provide a large margin of exposure (safety) from toxic effects. Taste and odor values are presented as a range, since human responses vary depending upon the sensitivities of the particular individual and the site-specific water quality conditions. These values are provided as guidance recognizing that water suppliers determine the level of treatment required for aesthetics based upon the customers they serve and the particular site-specific water quality conditions. There are over four to five orders of magnitude between the 20 to 40 µg/L range and concentrations associated with observed cancer and noncancer effects in animals. There is little likelihood that an MtBE concentration of 20 to 40 g/L in drinking water would cause adverse health effects in humans, recognizing that some people may detect the chemical below this range. It can be noted that at this range of concentrations, the margins of exposure are about 10 to 100 times greater than would be provided by an EPA reference dose (RfD) for noncancer effects. Additionally, they are in the range of margins of exposure typically provided by National Primary Drinking Water Standards under the Federal Safe Drinking Water Act to protect people from potential carcinogenic effects.
When adequate data become available, the Office of Water will publish another Advisory that includes quantitative estimates for health risks. This Advisory gives practical guidelines for addressing contamination problems and supersedes previous draft advisories. An Advisory does not mandate a standard for action.

Polystyrene, CAS #9003-53-6

Data Point	Data Summary	Reference
Water solubility	ND	
K_{oc}	ND	
Soil half-life	ND	
BCF	ND	
Ingestion toxicity	Not absorbed when administered orally to laboratory rats.	Monte 1983
Carcinogenicity	Subcutaneous implantation of polystyrene discs, rods, spheres or powder in rats induced local sarcomas, the incidences of which varied with the size and form of the implant.	IARC 1979
Fish toxicity	ND	
Aq. invert. tox	ND	
Aq. amph. tox	ND	

International Agency for Research on Cancer. 1979. Styrene, polystyrene, and styrene-butadiene compounds. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Volume 19:231. http://193.51.164.11/htdocs/monographs/vol19/styrene%26polymers.html

Monte, W. 1983. Lack of gut absorption of solubilized polystyrene by the rat (abstract). Journal of Agricultural and Food Chemistry 31(1):174-175.

International Agency for Research on Cancer. 1979. Styrene, polystyrene, and styrene-butadiene compounds. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Volume 19:231.

Evaluation

Although no information is available on carcinogenicity in humans attributable to styrene, its wide use and the facility with which it can be absorbed by inhalation indicate that it may be possible to carry out studies measuring both dose and cancer incidence in exposed workers. The finding of chromosomal aberrations in workers exposed to styrene further supports the need for epidemiological investigations.

Results from polystyrene implant studies in animals point to the need for further investigations with regard to the polymer. Recent epidemiological information on styrene-butadiene copolymer workers, which indicates lymphato-haematopoeietic malignancies, clearly requires elucidation by further studies.

Monte, W. 1983. Lack of gut absorption of solubilized polystyrene by the rat (abstract). Journal of Agricultural and Food Chemistry 31(1):174-175.

The absorption of solubilized polystyrene (9003536) was studied in rats. Carbon-14 labeled polystyrene, with a molecular weight range similar to that of commercial grades of expanded polystyrene, was dissolved in lemon oil. Male Long-Evans-rats were weighed and administered intragastrically 2 microCuries carbon-14 labeled polystyrene in 100 milliliter of lemon oil. Urine and feces were collected at 8 hour intervals. Weights, food eaten, and appearance of animals were recorded. Animals were killed 120 hours after polystyrene feeding. Samples of blood, skin, subcutaneous tissue, lungs and bronchi, trachea, bone marrow, spleen, lymph nodes, heart, liver, pancreas, stomach, large and small intestines, kidney, urinary bladder, testes, and brain were tested for carbon-14 activity. Urine and fecal material were tested by scintillation determination for carbon-14 activity. Rats appeared normal. None of the tissue samples showed any activity above background. Two urine samples, contaminated with fecal matter, showed slight activity. Within the bounds of experimental error, all the carbon-14 was found in the fecal samples and 99 percent was excreted within 48 hours after intubation. The author concludes that polystyrene solubilized in an absorbable solvent does not pass through the intestinal barrier of rats.

Potassium Chloride, CAS # 7447-40-7 (KCl), and Potassium Hydroxide, CAS # 1310-58-3 (KOH)

Data Point	Data Summary	Reference
Water solubility	281,000 mg/L (KCl) and 970,000 mg/L (KOH)	HSDB 2002
K_{oc}	No data.	
Soil half-life	No data.	
BCF	No data.	
Ingestion toxicity	Maximal nontoxic oral dose of KCl in man varies from 200 to 1,000 mg/kg/day, depending on efficiency of individual renal excretory mechanism. KOH is one of the strongest alkalies--it is extremely corrosive. Swallowing caustic alkalies causes immediate burning pain in the mouth, throat, and stomach, and the lining membranes become swollen and detached.	HSDB 2002
Carcinogenicity	No data.	
Fish toxicity	EPA has set an ambient water quality criteria level of 230 mg/L for chloride for the protection of freshwater aquatic life.	EPA 1999
Aq. invert. tox		
Aq. amph. tox		

EPA. See U.S. Environmental Protection Agency.

Hazardous Substances Databank. 2002. On-line database. National Library of Medicine. Bethesda, MD. http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB

HSDB. See Hazardous Substances Databank.

U.S. Environmental Protection Agency. 1999. National recommended water quality criteria--Correction. EPA 822-A-99-01. Office of Water. Washington, DC.

Hazardous Substances Databank. 2002. On-line database. National Library of Medicine. Bethesda, MD.

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The following is the HSDB summary of human health and environmental fate information:

HUMAN HEALTH EFFECTS:

HUMAN TOXICITY EXCERPTS:

LARGE DOSES BY MOUTH CAN CAUSE GI IRRITATION, PURGING, WEAKNESS AND CIRCULATORY DISTURBANCES. [The Merck Index. 9th ed. Rahway, New Jersey: Merck & Co., Inc., 1976. 990]**PEER REVIEWED**

AN 84-YR-OLD WOMAN WITH...MANY EPISODES OF CONGESTIVE FAILURE WAS IN... CONTROLLED CARDIAC STATUS WHEN SHE COMMITTED SUICIDE BY INGESTING...LIQ POTASSIUM SUPPLEMENT. EST DOSE...(EQUIV TO ABOUT 40 TO 50 G KCL)... GRAND MAL CONVULSION OCCURRED AFTER 1 HR FOLLOWED BY COMA...BLOOD PRESSURE WAS UNOBTAINABLE. /POTASSIUM SALTS/ [Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984.,p. II-124]**PEER REVIEWED**

NAUSEA, VOMITING, DIARRHEA, & ABDOMINAL DISCOMFORT COMMONLY OCCUR. OVERDOSES MAY CAUSE PARESTHESIAS, GENERALIZED WEAKNESS, FLACCID PARALYSIS,
LISTLESSNESS, VERTIGO, MENTAL CONFUSION, HYPOTENSION, CARDIAC ARRHYTHMIAS, & HEART BLOCK. DEATH MAY ENSUE. [Osol, A. and J.E. Hoover, et al. (eds.). Remington's Pharmaceutical Sciences. 15th ed. Easton, Pennsylvania: Mack Publishing Co., 1975. 771]**PEER REVIEWED**

ACUTE POTASSIUM INTOXICATION BY MOUTH IS RARE BECAUSE LARGE SINGLE DOSES USUALLY INDUCE VOMITING AND BECAUSE IN THE ABSENCE OF PRE-EXISTING KIDNEY DAMAGE POTASSIUM IS RAPIDLY EXCRETED. /POTASSIUM SALTS/ [Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984.,p. II-124]**PEER REVIEWED**

Potassium chloride in a commercial dietary salt substitute ... has produced a near fatal poisoning in an 8 month old infant. [Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984.,p. II-124]**PEER REVIEWED**

MAXIMAL NONTOXIC ORAL DOSE OF KCL IN MAN VARIES FROM 0.2 TO 1.0 G K/KG/DAY, DEPENDING UPON EFFICIENCY OF INDIVIDUAL RENAL EXCRETORY MECHANISM; LOWER DOSES SOMETIMES CAUSE IMPAIRMENT OF RENAL FUNCTION AS SHOWN BY REDUCED INULIN & UREA CLEARANCE. ... SERUM K LEVEL OF 40 MG/100 ML IS FATAL IN MAN. [Venugopal, B. and T.D. Luckey. Metal Toxicity

in Mammals, 2. New York: Plenum Press, 1978. 16]**PEER REVIEWED**

ENVIRONMENTAL FATE & EXPOSURE:

NATURAL POLLUTION SOURCES:
A main commercial product is sylvite, KCl [Harben PW, Bates RL; Geology of the Nonmetallics, p.246 (1984)]**PEER REVIEWED**

KCl makes up 4% of the salts in the Great Salt Lake; present in the Bonneville Salt Flats and Searles Lake & the Paradox Basin [Harben PW, Bates RL; Geology of the Nonmetallics, p.246 (1984)]**PEER REVIEWED**

U.S. Environmental Protection Agency. 1999. National recommended water quality criteria--Correction. EPA 822-A-99-01. Office of Water. Washington, DC.

SUMMARY: EPA is publishing a compilation of its national recommended water quality criteria for 157 pollutants, developed pursuant to section 304(a) of the Clean Water Act (CWA or the Act). These recommended criteria provide guidance for States and Tribes in adopting water quality standards under section 303(c) of the CWA. Such standards are used in implementing a number of environmental programs, including setting discharge limits in National Pollutant Discharge Elimination System (NPDES) permits. These water quality criteria are not regulations, and do not impose legally binding requirements on EPA, States, Tribes or the public.

Silicon Dioxide, CAS #7631-86-9 (silica)

Data Point	Data Summary	Reference
Water solubility	Practically insoluble.	HSDB 2002
K_{oc}	Not applicable.	
Soil half-life	Stable (occurs as sand and quartz).	HSDB 2002
BCF	None.	
Ingestion toxicity	When male and female beagle dogs or CD rats were fed 800 mg silicon/kg/day as the dioxide for 1 month ... neither clinical signs of toxicity nor histologic changes were seen in these animals. It is chemically and biologically inert when ingested. It is approved for use in food products at levels up to 2%, and is Generally Recognized as Safe (GRAS).	HSDB 2002, EPA 2002
Carcinogenicity	Crystalline silica is carcinogenic.	HSDB 2002, EPA 1991
Fish toxicity	Chemically unreactive in the environment, occurs naturally in various forms and is practically non-toxic to non-target organisms.	EPA 1991
Aq. invert. tox		
Aq. amph. tox		

EPA. See U.S. Environmental Protection Agency.

Hazardous Substances Databank. 2002. On-line database. National Library of Medicine. Bethesda, MD. http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB

HSDB. See Hazardous Substances Databank.

U.S. Environmental Protection Agency. 1991. Reregistration eligibility document: Silicon dioxide and silica gel. Office of Pesticide Programs. Washington, DC. http://www.epa.gov/oppsrrd1/REDs/old_reds/4081red.pdf

Hazardous Substances Databank. 2002. On-line database. National Library of Medicine. Bethesda, MD.

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The following is the HSDB summary of human health and environmental fate information:

Human Health Effects:

Human Toxicity Excerpts:

The details of toxicity associated with metallurgical silicon are unknown.
[Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984.,p. V20 851 (1982)]**PEER REVIEWED**

Nuisance particulate (accumulation in lungs).
[Cralley, L.J., L.V. Cralley (eds.). Patty's Industrial Hygiene and Toxicology. Volume III: Theory and Rationale of Industrial Hygiene Practice. 2nd ed., 3A:The Work Environment. New York, NY: John Wiley Sons, 1985. 181]**PEER REVIEWED**

... Increased renal silicon (200 ppm dry weight; normal = 14-23 ppm) /was found/in an adult male bricklayer who presented with proteinuria and hypertension, but who had a normal chest roentgenogram. Moderate thickening of the glomerular basement membrane was noted on transmission electron microscopy.
[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. 1387]**PEER REVIEWED**

Skin, Eye and Respiratory Irritations:

Unpleasant deposits /of silicon dust/ in eyes, ears & nasal passages & injury to the skin and mucous membranes may be caused by the dust itself or by cleansing procedures used for its removal.
[Sittig, M. Handbook of Toxic and Hazardous Chemicals and Carcinogens, 1985. 2nd ed. Park Ridge, NJ: Noyes Data Corporation, 1985. 787]**PEER REVIEWED**

Environmental Fate & Exposure:

Natural Pollution Sources:

Silicon is not found free in nature, but occurs chiefly as the oxide, & as silicates. Sand, quartz, rock crystal, amethyst, agate, flint, jasper, & opal are some of the /oxide/ forms. Granite, hornblende, asbestos, feldspar, clay, mica ... are but a few of the numerous silicate minerals.
[Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 73rd ed. Boca Raton, FL: CRC Press Inc., 1992-1993.,p. 4-26]**PEER REVIEWED**

THREE NATURALLY OCCURRING ISOTOPES: 28 (92.18%); 29 (4.71%); 30 (3.12%) ... FOUND ASSILICA (... SANDSTONE) OR AS SILICATE (... ORTHOCLASE, KAOLINITE, ANORTHITE). CONSTITUTES ABOUT 27.6% OF EARTH'S CRUST; SECOND MOST ABUNDANT ELEMENT ON EARTH ... .
[Budavari, S. (ed.). The Merck Index - Encyclopedia of Chemicals, Drugs and Biologicals. Rahway, NJ: Merck and Co., Inc., 1989. 1346]**PEER REVIEWED**

U.S. Environmental Protection Agency. 1991. Reregistration eligibility document: Silicon dioxide and silica gel. Office of Pesticide Programs. Washington, DC.

This Reregistration Eligibility Document addresses both silicon dioxide and silica gel. Silicon dioxide is essentially an inert material that contains approximately 90% silica. It is commonly used as an inert carrier in dry concentrates, dry pesticides, as an anti-caking agent, soil conditioner and turf soil supplement and occasionally used as an active ingredient. Silicon dioxide's most common insecticidal use today is for control of stored grain insects. It is also registered for use to control a variety of insects/mites in and around domestic/commercial dwellings, ornamental gardens, in kennels and on domestic pets. Silica gel is a registered insecticide and acaricide for use to control a variety of insects in and around residences/commercial dwellings, agricultural premises, institutions, warehouses, food plants, livestock, cat, dogs and in granaries. Because of their abrasive characteristics both active ingredients act on insects by removing the oily protective film covering their bodies which normally prevents the loss of water. Thus the mode of action is physical in nature causing
desiccation of the insect. Both active ingredients are usually combined with other pesticides which act as a knockdown agent. All products which contain silicon dioxide and silica gel registered for these uses are eligible for reregistration.

The U. S. Environmental Protection Agency (EPA) conducted a review of the scientific data base and other relevant information supporting the reregistration of silicon dioxide and silica gel and has determined that the data base is sufficient to conduct a reasonable risk assessment. In addition, the Agency has conducted a tolerance reassessment for silicon dioxide and silica gel and its conclusions are discussed in Section IIC. The data available to the EPA support the conclusion that the currently registered uses of silicon dioxide and silica gel will not result in unreasonable public health risks or effects to the environment. No further generic data are required.

Accordingly, the EPA has determined that all products containing silicon dioxide and silica gel as the active ingredients are eligible for reregistration and will be reregistered when appropriate labeling and/or product specific data are submitted and/or cited. Before reregistering each product, the EPA is requiring product specific data to be submitted within eight months of the issuance of this document. After reviewing these data and the revised labels, the EPA will determine whether to reregister a product based on whether or not the conditions of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) Section 3(c)(5) have been met. End use products containing silicon dioxide and silica gel in combination with other active ingredients will not be reregistered until those other active ingredients are determined to be eligible for reregistration. However, product specific data are being called in at this time.

Strontium Oxides and Sulfate, CAS # 1314-11-0 (strontium oxide, SrO), 1314-18-7 (strontium peroxide, SrO_2), 7759-02-6 (strontium sulfate, $SrS0_4$)

Data Point	Data Summary	Reference
Water solubility	SrO forms the hydroxide with evolution of heat in presence of water. SrO_2 is almost insoluble in water, but is gradually decomposed by water with the evolution of oxygen. $SrSO_4$ is soluble in water at about 114 mg/L.	Budavari et al. 1989
K_{oc}	The distribution coefficient, K_d (amount of ion per kg of air dry soil/amount of ion per liter of soil solution), for strontium in a podsol forest soil was determined to be 140 L/kg in the top layer and 44 L/kg in the lower layer.	HSDB 2002
Soil half-life	No data.	
BCF	BCF of strontium was 576 to 1,286 in bluegill sunfish.	HSDB 2002
Ingestion toxicity	The strontium ion has a low order of toxicity. It is chemically and biologically similar to calcium. The oxides are moderately caustic materials. The human daily intake of strontium has been determined to be 2 mg. An oral reference dose of 0.6 mg/kg/day was estimated for stable strontium. An oral rat LD_{50} of 2,750 mg/kg was identified for strontium nitrate Sr(NO3)2. This is equivalent to an LD_{50} of 1,139 mg strontium/kg.	Lewis 1994 HSDB 2002 EPA 1996 Oxford 2002
Carcinogenicity	No data.	
Fish toxicity	A 96-hour LC_{10} of 0.049 mg/L was identified for Sr for newly hatched rainbow trout.	EPA 2002
Aq. invert. tox	No data.	
Aq. amph. tox	7-day LC_{50} for Sr in eastern narrowmouth toad embryo-larvae was 0.16 mg/L	Pauli et al. 2000

Budavari, S., M. O'Neil, A. Smith, and P. Heckelman, eds. 1989. *The Merck Index: An Encyclopedia of Chemicals, Drugs, and Biologicals.* 11th ed. Merck & Co., Inc. Rahway, NJ.

EPA. See U.S. Environmental Protection Agency.

Hazardous Substances Databank. 2002. On-line database. National Library of Medicine. Bethesda, MD. http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB

HSDB. See Hazardous Substances Databank.

Lewis, R. 1994. *Sax's Dangerous Properties of Industrial Materials*. 8th ed. Van Nostrand Reinhold Company. New York.

Oxford University. 2002. Safety data for strontium nitrate. The Physical and Theoretical Chemistry Laboratory. http://physchem.ox.ac.uk/MSDS/ST/strontium_nitrate.html

Pauli, B.D., J.A. Perrault, and S.L. Money. 2000. RATL: A database of reptile and amphibian toxicology literature. Technical Report Series No. 357. Canadian Wildlife Service, Headquarters, Hull, Québec, Canada. http://www.cws-scf.ec.gc.ca/nwrc/ratl/about_e.htm

U.S. Environmental Protection Agency. 1996. Integrated risk information system. Office of Research and Development. Cincinnati, OH. http://www.epa.gov/iris/subst/0550.htm

U.S. Environmental Protection Agency. 2002. Ecotox database: Lead. Mid-Continent Ecology Division, National Health and Environmental Effects Research Laboratory, Office of Research and Development. Duluth, MN. http://www.epa.gov/ecotox/

Hazardous Substances Databank. 2002. On-line database. National Library of Medicine. Bethesda, MD.

HSDB is a toxicology data file on the National Library of Medicine's (NLM) Toxicology Data Network (TOXNET®). It focuses on the toxicology of potentially hazardous chemicals. It is enhanced with information on human exposure, industrial hygiene, emergency handling procedures, environmental fate, regulatory requirements, and related areas. All data are referenced and derived from a core set of books, government documents, technical reports and selected primary journal literature. HSDB is peer-reviewed by the Scientific Review Panel (SRP), a committee of experts in the major subject areas within the data bank's scope. HSDB is organized into individual chemical records, and contains over 4500 such records.

The following is the HSDB summary of human health and environmental fate information:

HUMAN HEALTH EFFECTS:

HUMAN TOXICITY EXCERPTS:

The toxicity of strontium compounds depends on the anion. /Strontium/ [Seiler, H.G., H. Sigel and A. Sigel (eds.). Handbook on the Toxicity of Inorganic Compounds. New York, NY: Marcel Dekker, Inc. 1988. 633]**PEER REVIEWED**

ACCIDENTAL INGESTION MAY CAUSE GASTROINTESTINAL DISORDERS, PAINFUL CONTRACTIONS IN LIMBS ... /STRONTIUM AND COMPOUNDS/ [International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 2111]**PEER REVIEWED**

The hazard of (90)Sr is primarily that of internal contamination. In the body it is deposited mainly in the bones & due to its long biological half-life, it may result in beta-ray induced hemopoietic tissue lesions & malignant bone growth. /(90)Sr/ [International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. 2112]**PEER REVIEWED**

This isotope /(90)Sr/ ... has been implicated as a causative agent in ... leukemia. /(90)Sr/ [National Research Council. Drinking Water & Health, Volume 4. Washington, DC: National Academy Press, 1981. 189]**PEER REVIEWED**

PROBABLE ROUTES OF HUMAN EXPOSURE:

NIOSH (NOES Survey 1981-1989) has statistically estimated that 2,991 workers (35 of these are female) are potentially exposed to strontium in the US(1). Occupational exposure to strontium may occur through inhalation of this compound at workplaces where strontium is produced or used(SRC). The general population may be exposed to strontium via inhalation of ambient air and ingestion of drinking water and milk containing strontium(SRC). [(1) NIOSH; National Occupational Exposure Survey (NOES) (1983)]**PEER REVIEWED**

ENVIRONMENTAL FATE/EXPOSURE SUMMARY:

Strontium forms 0.02-0.03% of the earth's crust and is present in igneous rocks in amounts averaging 375 ppm. Of the naturally occurring strontium

compounds, only the minerals strontianite (strontium carbonate) and celestite (strontium sulfate) are of economic importance. Of the two, celestite occurs much more frequently in sedimentary deposits of sufficient size to make development of mining facilities attractive. Strontium is the fifth most abundant metallic ion in seawater, occurring in quantities of approximately 14 grams per metric ton. More than 80% of all strontium consumed in 1995 was used in ceramic and glass manufacture, primarily in televison faceplate glass (strontium carbonate/oxide) and ceramic ferrite magnets (strontium ferrite). Because of its brilliant red flame, strontium (in particular, strontium nitrate) is used in pyrotechnic devices for the military (tracer ammunition, military flares, marine distress signals) as well as non-military applications including warning devices and fireworks. In addition, strontium (strontium carbonate) is used to remove lead impurities during the electrolytic production of zinc, as an additive to corrosion resistant paint (strontium chromate), in toothpaste for temperature-sensitive teeth (strontium chloride), and in the manufacture of fluorescent lights (strontium phosphate). In addition, strontium-90 has been distributed worldwide by the fallout of nuclear explosions during the 1960's and the fallout of the Chernobyl, U.S.S.R., accident in 1986; most of the radioactive strontium was sorbed in top soil layers. The concn of strontium sorbed in 21 natural sediment-groundwater systems was determined to range from 9.2X10-7 to 1.04X10-4 mole/cu-dm; the main parameters governing strontium sorption were cation-ion exchange capacity of the sediment and ionic strength of the groundwater. The distribution coefficient, Kd, for strontium in a podsol forest soil was determined to be 140 l/kg in the top layer and 44 l/kg in the lower layer. Volatilization from soil surfaces will not be an important fate process. Strontium compounds are expected to exist primarily in the particulate-phase in the ambient atmosphere. Particulate-phase strontium may be physically removed from the air by wet or dry deposition. Volatilization of the ionic form of strontium from water surfaces will not occur. Bioconcentration of strontium in bluegill fish (Lepomis macrochirus) was determined to range from 1.4-1286.0 in fish collected from the Merced River and Salt Slough, CA. Occupational exposure to strontium may occur through inhalation of this compound at workplaces where strontium is produced or used. The general population may be exposed to strontium via inhalation of ambient air and ingestion of drinking water and milk containing strontium. (SRC) **PEER REVIEWED**

Lewis, R. 1994. *Sax's Dangerous Properties of Industrial Materials*. 8th ed. Van Nostrand Reinhold Company. New York.

STRONTIUM COMPOUNDS
DPIM: SMH500 Hazard Rating: 1
SAFETY PROFILE:
The strontium ion has a low order of toxicity. It is chemically and biologically similar to calcium. Strontium salicylate is the most toxic compound. The oxides and hydroxides are moderately caustic materials. Symptoms of acute toxicity are excessive salivation, vomiting, colic, and diarrhea, and possibly respiratory failure. The gastrointestinal absorption of soluble strontium ranges from 5 to 25%. Workers in strontium salt plants have reduced activity of choline esterase and acetylcholine. Drinking water with 13 mg Sr/L caused impaired tooth development in 1-year-old children. As with other compounds, the toxicity of a given compound may be a function of the anion. Compounds are highly dangerous if they contain the radioactive isotope 90Sr.
Updated: 08/27/90

Pauli, B.D., J.A. Perrault, and S.L. Money. 2000. RATL: A database of reptile and amphibian toxicology literature. Technical Report Series No. 357. Canadian Wildlife Service, Headquarters, Hull, Québec, Canada.

The RATL (Reptile and Amphibian Toxicology Literature) database contains data extracted from the primary literature for amphibian and reptile ecotoxicology studies published up to and including 1997; there are some data from studies published in 1998 and 1999. As of September, 2000, there was approximately 2000 references in the database. Citations were gathered through searches of various literature databases, but these searches concentrated on the environmental pollution literature with the result that the bibliography cannot be considered exhaustive.

U.S. Environmental Protection Agency. 1996. Integrated risk information system. Office of Research and Development. Cincinnati, OH.

I.A. REFERENCE DOSE FOR CHRONIC ORAL EXPOSURE (RFD):

:

Substance Name -- Strontium
CASRN -- 7440-24-6

Last Revised -- 12/01/1996

I.A.1. ORAL RFD SUMMARY:

Critical Effect	Experimental Doses*	UF	MF	RfD
Rachitic bone	NOAEL: 0.19% Sr (as SrCO3) (190 mg Sr/kg/day)	300	1	6E-1 mg/kg/day

U.S. Environmental Protection Agency. 2002. Ecotox database: Lead. Mid-Continent Ecology Division, National Health and Environmental Effects Research Laboratory, Office of Research and Development. Duluth, MN.

The ECOTOXicology database is a source for locating single chemical toxicity data for aquatic life, terrestrial plants and wildlife. ECOTOX integrates three toxicology effects databases: AQUIRE (aquatic life), PHYTOTOX (terrestrial plants), and TERRETOX (terrestrial wildlife). These databases were created by the U.S. EPA, Office of Research and Development (ORD), and the National Health and Environmental Effects Research Laboratory (NHEERL), Mid-Continent Ecology Division.

Scientific name, Common name	Endpoint	Effect	Trend -------- - Effect %	Media Type	Duration ---------- Exp Typ	Conc (ug/L)	Signif ------- Level	Response Site ------- BCF	Ref #
Oncorhynchus mykiss Rainbow trout, donaldson trout	LC10	MOR	INC --------	FW	4 dph ----------	T 49.0		------	14527