ARCS

Remedial Planning Activities at Selected Uncontrolled Hazardous Substance Disposal Sites in Region I

Burgess Bros.
3.10

Environmental Protection Agency
Region I

ARCS Work Assignment No. 26-1BB5

Risk Assessment
Burgess Brothers Superfund Site
Woodford and Bennington, Vermont

April 1997

Volume 2 of 2

TRC Companies, Inc.

TAMS Consultants, Inc.
PEI Associates, Inc.
Jordan Communication

MS8471/S

4040

000043

SDMS Doc ID 4040

APPENDIX C

TOXICITY PROFILES

VOLATILES

BENZENE

Use

Benzene is a clear, colorless, aromatic hydrocarbon that possesses a distinct sweet odor (NIOSH, 1987). It is extremely flammable and volatile. Benzene is widely used in the production of other industrial compounds, such as styrene and phenols, and in making common household materials such as rubber, plastic, and inks (Sittig, 1991). Exposure to the public is mainly through the combustion of gasoline and through cigarette smoke.

Chemical and Physical Properties

Chemical Formula: $C_6 H_6$

MW:	78	BP:	80.1°C
SG:	0.879 at 20°C	MP:	5.56°C
FP:	-11.1°C	VP:	100 mmhg at 26°C

Sol. (water): 1780 mg/l at 25°C

Sol. (organics): Miscible with ethanol, ether acetic acid, acetone, chloroform, carbon disulfide, and carbon tetrachloride.

Odor Threshold: 2 ppm (EPA, 1985)

Fate and Transport

Because of its volatility, benzene is photo-oxidized very rapidly in the atmosphere, with a half-life of less than 1 day (EPA, 1985). In moist soils, benzene is retained and slowly transported into the ground water, where it is known to remain stable (EPA, 1985). The bioaccumulation of benzene appears to be relatively low.

Pharmacokinetics

Benzene is highly lipid soluble and is readily absorbed via inhalation, ingestion, and dermal contact. Approximately 50 percent of benzene is absorbed through inhalation. Absorbed benzene is readily distributed to fatty tissues where it is sequestered. The prime target organ is the bone marrow. Detoxification of bodily fluids occurs in the liver. The major metabolite of benzene in humans is phenol sulfite, but it can also be excreted unchanged.

Human Toxicity

Noncarcinogenic Effects

Systemic Effects

Target organs of benzene include bone marrow, central nervous tissues, and the respiratory system (NIOSH, 1987).

In a work environment, benzene can be acutely fatal to humans in extremely high concentrations (20,000 ppm) and can cause short-term effects such as dizziness and vomiting in humans exposed to lower levels (Sittig, 1991).

In elevated concentrations, benzene can be fatal within minutes (EPA, 1985). Initially, benzene causes central nervous system depression, followed by acute arrythmia and cardiovascular collapse. If benzene in a liquid state is aspirated into the lung, immediate pulmonary edema and hemorrhaging can occur (Sittig, 1991). Benzene is known to cause aplastic anemia, leukopenia, and thrombocytopenia in humans as a result of chronic exposure. The latency period can be as long as 10 years (Sittig, 1991).

Both gavage and inhalation exposure of rodents to benzene have resulted in the development of neoplasia. The incidence of tumors, carcinomas, leukemias, and lymphomas have been shown to be directly proportional to the dosage administered. (EPA, 1985).

Teratogenic and Other Developmental Effects

Benzene is known to be a potent inhibitor of growth *in utero*. It has also been shown to cause chromosomal aberrations in the bone marrow cells of workers as a result of chronic exposure (EPA, 1985).

Pregnant mice were given gavage doses of benzene at levels between 0.3 and 1.0 mg/kg daily on days 6-15 of gestation. Increased mortality among the dams and resorption of embryos occurred for all levels (EPA, 1984). No teratogenic effects were noted in rabbits, rats, or fruit flies exposed to less than 550 ppm in the air.

Mutagenic Effects

Signs of mutagenicity amongst rabbits, mice, rats, and fruit flies were not seen when they were exposed to benzene levels of 550 ppm in the air.

Carcinogenic Effects

Benzene is classified as a Class A human carcinogen. Aksoy, et al. reported effects of benzene exposure among 28,500 Turkish employed in the shoe industry. The peak exposure was reported to be 210-650 ppm over a period of 10 years. An incidence of 13/100,000 cases was reported for the workers, compared to 6/100,000 for the general public (IRIS).

In a second study, the effects of benzene exposure on 748 white males employed in a rubber manufacturing industry were examined.. A statistically significant increase in the mortality rate due to leukemia was noted for the population. There was no evidence of exposure to solvents other than benzene (IRIS).

Rinsky, et al. (1981) noted a statistically significant increase in the number of leukemia deaths in workers occupationally exposed to benzene. Exposure was estimated to be between 10 and 100 ppm, 8-hour TWA. Ott, et al. (1978) noted an increase in leukemia deaths in workers exposed to between 2 to 25 ppm, 8-hour TWA. The increase, however, was determined by EPA to be insignificant (IRIS, 1990). Wong, et al. (1983) noted statistically significant increases in leukemias, lymphatic, and hematopoietic cancers in chemical plant workers exposed to benzene for at least 6 months. No statistical details were reported (IRIS).

Benzene was shown to have caused leukemia directly, or as a result of bone marrow abnormalities in Sprague-Dawley rats (Maltoni and Scartano, 1979). Benzene was administered by gavage at doses of 50 and 250 mg/kg bw for 4 to 5 days/week for 52 weeks. Twenty five percent developed Zymbal gland tumors, 6.2 percent had skin carcinomas, and 12.1 percent had leukemias at the end of the 52 weeks (IRIS). Dogs exposed to 600 to 1000 ppm benzene for 12-15 days also developed leukemia (EPA, 1985).

Ecotoxicity

In aquatic toxicity bioassays, the EC_{50} values for benzene in a variety of invertebrate and vertebrate freshwater aquatic species range between 5300 µg/L and 386,000 µg/L. In these studies, however, only those performed on rainbow trout were obtained from a flow through test and were based on measured concentrations. Results based on unmeasured concentrations in static tests are likely to underestimate the toxicity for relatively volatile compounds, such as benzene. A chronic test on *Daphnia magna* was determined to be incomplete, however in this test, no adverse effects were observed at test concentrations as high as 98,000 µg/L (EPA, 1980).

Standards, Criteria and Guidelines

EPA Class A carcinogen

Oral Slope Factor:	2.9×10^{-2} (mg/kg/day)$^{-1}$
Inhalation Slope Factor:	2.9×10^{-2} (mg/kg/day)$^{-1}$
Chronic Oral RfD:	NA
Chronic Inhalation RfD:	NA
Subchronic Oral RfD:	NA
MCL:	5.0 µg/L

BIBLIOGRAPHY

Aksay, M. et al. Leukemia in shoeworkers exposed chronically to benzene. *Blood.* 44(6): 837-841, 1974 (Cited in IRIS).

Maltoni, C. and C. Scarnato, First Experimental Demonstration of the Carcinogenic Effects of Benzene, Long Term Bioassays on Sprague-Dawley Rats by Oral Administration, *Med. Lav.*, 70: 352-357, 1979, (Cited in EPA, 1985).

NIOSH, *Pocket Guide to Chemical Hazards*, 1987.

Ott, M.G., J.C. Townsend, W.A. Fishbeck and R.A. Laugner, Mortality Among Individuals Occupationally Exposed to Benzene, 1978, *Arch. Environ. Health*, 33:3-10, (Cited in IRIS). Rinsky, R.A., R.J. Young and A.B. Smith, Leukemia in Benzene Workers, 1981, *Am. J. Ind., Med.*, 2: 217-245, (Cited in IRIS).

Sittig, Marshall, *Handbook of Toxic and Hazardous Chemicals*, 1991.

U.S. EPA, Ambient Water Quality Criteria for Benzene, 1980.

U.S. EPA, *Drinking Water Regulations and Health Advisories.*

U.S. EPA, Environmental Criteria and Assessment Office, *Health Effects Assessment for Benzene*, EPA 540/1-86/037, September 1984.

U.S. EPA, *Integrated Risk Information System (IRIS).*

U.S. EPA, OERR. *CERCLA Compliance with Other Laws Manual Interim Final.* August, 1988.

U.S. EPA, Office of Drinking Water, *Advisory Opinion for Benzene* (undated).

U.S. EPA, Office of Drinking Water, *Health Advisory,* September 30, 1985.

CARBON DISULFIDE

Use

Carbon disulfide is also known as carbon bisulfide and dithiocarbonic anhyride (U.S. EPA, 1985). It is a clear, colorless, very flammable and highly volatile liquid that has a mild, ethereal order when pure, but a disagreeable sulfurous odor when impure (Timmerman, 1978). Carbon disulfide is produced by high temperature reaction of methane and sulfur gas in the presence of a catalyst such as charcoal, Cr, W, and Mo compounds, and oxides, sulfides of metals (Timmerman, 1978). It is used in the manufacture of rayon, cellophane, carbon tetrachloride (Timmerman, 1978) and a variety of other uses including manufacture of rubber chemicals and flotation agents, ammonium thiocyanate, sodium thiocyanate, xanthogenates, electronic vacuum tubes, use as an insecticide (fumigant) and as a solvent for phosphorus, sulfur, selenium, bromine, iodine fats, resins, and rubber (CMR, 1983; Berg, 1981; Windholz, 1983).

Chemical and Physical Properties

Chemical Formula: CS_2

MW: 76.13		BP:	46.3°C
Sol. (water):	2,940 mg/liter	MP:	-108.6 to -116.6°C
Sol. (organics):	miscible with anhydrous methanol, ethanol, ether, benzene, chloroform, carbon tetrachloride, and oil	VP:	297 mmHg at 20°C

Fate and Transport

In aquatic media, hydrolysis of carbon disulfide is not an environmentally significant event (Peyton et. al., 1978). Peyton et. al. (1978) estimated the evaporation $t_{1/2}$ of carbon disulfide from saturated water to be 11 minutes. U.S. EPA (1986) states the volitization should be a rapid and important removal process based on Henry's Law constant. It appears from BCF estimations that carbon disulfide will not bioaccumulate (U.S. EPA, 1986).

Atkinson et. al. (1978) and Wood and Heicklen (1971) found that carbon disulfide does not photolyze directly under atmospheric conditions. The U.S. EPA (1986) reports that experimental data indicate that carbon disulfide is removed from the troposphere before it can enter the stratosphere.

Being a soil disinfectant, carbon disulfide is unlikely to biodegrade significantly in soils and hydrolysis on wet soil surfaces is also unlike (U.S. EPA, 1986). The expected volatilization of carbon disulfide from water suggests that this may be a major escape route from soils as well (U.S. EPA, 1986). In a study of the adsorption gaseous carbon disulfide onto soils, Bremner and Banwart (1976) suggest that soils have little if any potential for removing carbon disulfide from industrial emissions.

Pharmacokinetics

Numerous studies have shown that carbon disulfide is absorbed extensively from the lungs in humans and animals and that a steady-state is achieved between inhaled and exhaled carbon disulfide within one to two hours of exposure (U.S. EPA, 1986). Carbon disulfide and its metabolites were distributed rapidly to body fat and highly perfused tissues in studies on rats and mice by McKenna and DiStefano (1977) and Bergman et. al. (1984). It was also reported that free carbon disulfide is eliminated more rapidly from the tissues than its metabolites (McKenna an DiStefano, 1977). Bioacumulation in any tissue does not appear significant for free carbon disulfide or its metabolites (U.S. EPA, 1986).

The U.S. EPA (1986) reported on numerous studies that suggest two major routes for the metabolism of carbon disulfide: reaction with amino acids or reduced glutathione to form thiocarbamates or conjugated glutathione, and by reactions catalyzed by cytochrome P450 to form reactive sulfur which may react further to form thiourea, carbonyl sulfide, or monothiocarbonate.

Excretion of carbon disulfide occurs rapidly in expired air, urine and milk (U.S. EPA, 1986). Numerous studies have shown that unchanged carbon disulfide is eliminated principally through the lungs with a small percentage being eliminated in the urine while its metabolites are excreted more slowly and primarily through the urine (U.S. EPA, 1986).

Human Toxicity

Noncarcinogenic Effects

Systemic Effects

Pilarska et. al. (1973) exposed 13 Wistar rats to 25 mg/kg/day carbon disulfide in arachis oil for 60 days. Carbon disulfide-exposed rats had normochromic and normocytic anemia, eosinopenia, and reticulocytosis. Dietzmann and Laas, as cited by U.S. EPA (1986), examined the tissues of the brain and spinal cord of male Wistar rats historically to study the effects of carbon disulfide on the CNS. The rats were treated by gavage with 0.06 ml carbon disulfide/rat twice weekly for eight weeks and then twice weekly with 0.12 ml carbon disulfide/rat for an additional 12 weeks. Exposed rats were killed at 4, 8, 12, 16, and 20 weeks. During the first few weeks, rats exhibited disorientation and a "reeling gait" that disappeared after three weeks. Hair loss occurred at 12 weeks and after 16 weeks of treatment, paraplegia of the hind and fore limbs occurred in "several animals". Histologically; destruction of ganglion cells in the cerebrum, cerebellum, and brain stem; elective parenchymal necrosis in frontal and parietal cortices; "micro-maculated fresh hemorraghic extravasates in the areas of nucleus rubber and pans"; and axonal swelling and destruction of the myelin sheath occurred after 12 weeks. Enzymatic changes (reductions in activities of succinic dehydrogenase and acetylcholinesterase, arylsulfatases, and glutamic dehydrogenase) occurred only after 20 weeks.

The U.S. EPA (1986) reports that occupational exposure to carbon disulfide has been associated with cardiovascular, neurologic, immunologic and ocular effects. They also report that animal studies have demonstrated neurologic, cardiovascular, hepatic, renal, gastrointestinal, and hematological effects caused by inhalation of carbon disulfide.

Vigliani (1954) reported that exposure to carbon disulfide at 144-321 ppm may cause psychosis, polyneuritis (absent of weakened achilles or patellar reflexes) tremors, weakness of limbs, myopathy and vertigo in a study from the viscose rayon industry.

Teratogenic and Other Development Effects

Jones-Price et. al. (1984a,b) exposed pregnant CD rats and New Zealand White Rabbits to carbon disulfide in corn oil by gavage. CD rats were exposed to 0, 100, 200, 400, or 600 mg/kg/day for days 6-15 of gestation and killed on day 20. Rabbits were exposed to 0, 25, 75, or 150 mg/kg/day on days 6-19 of gestation and killed on day 30. Maternal toxicity effects (abnormal posture, rigidity or paralysis of hind limbs, ataxia, lethargy, rough or erect coat, decreased body weight, decreased gravid uterine weight, increased liver weight), occurred in rabbits at 75 and 150 mg/kg/day and in rats at all doses, with the most severe effects of 400 and 600 mg/kg/day. Rats exhibited no compound-related effects on number of implants/litter, proportion of litters with deal, resorbed or affected fetuses, percent resorbed, dead or affected fetuses/litter, number of live fetuses/live litter, and percent males/live litter. They did exhibit a significant dose-related decrease in average fetal body weight/litter. The rabbits exposed to 150 mg/kg/day exhibited an increase in percent resorbtions (litter and percent malformations/litter). The U.S. EPA (1986) states that a significantly increased number of resorptions/litter in rabbits at a level where no maternal toxicity occurred (25 mg/kg/day) suggests that ingested carbon disulfide may have a primary effect on the developing fetus.

Gondzik (1971) exposed "mongrel" rats to 12.5 mg/kg or 25 mg/kg distilled carbon disulfide dissolved in peanut oil intraperitoneally every second day for 60 days or 120 days. Rats exposed to 12.5 mg/kg/2 days for 60 days showed no testicular effects. Those exposed to 25 mg/kg/2 days for 60 days exhibited thickened vascular walls in the testis vessels engorged with RBCs, disorganization of the layers of seminiferous epithelium, and a reduction in the number of spermatozoa in the tubular lumen. Rats exposed to this higher dose for 120 days exhibited advanced regressive lesions involving all structural parts of the testis; including folding and shrinking of the tubular basement membrane, scant stomal tissue, and loss of spermatogonia. Spermatogenesis was absent but Sertoli cells were present in every tubule. The number of leydig cells in the intertubular spaces was reduced and the cells showed signs

of degenerative vacuolation. The authors suggest that the nature of these effects indicate irreversibility.

Mutagenic Effects

Hedenstedt et. al. (1979) found that carbon disulfide was not mutagenic in bacterial reverse mutation assays with *Salmonella typhimurium* strain TA100 with or without S-9. Donner et. al. (1981) reported similar results for strains. TA98 and TA100 and Haworth et. al. (1983) also had similar results for strains TA98, TA100, TA1535, and TA1537. Donner et. al. (1981) also reported negative results in sex-linked recessive lethal studies in *Drosophila melanogaster* and Beliles et. al. (1980) reported a lack of mutagenicity in bone marrow cytogenesis and in dominant-lethal studies in rats.

Carcinogenic Effects

Checkoway et. al. (1984) and Wilcosky et. al. (1984) reported an association between lymphocytic leukemia and multiple solvent exposure. Eleven male hourly workers from the U.S. rubber industry whose deaths were attributed to lymphocytic leukemia were compared to a control group. Of the 24 solvents, the workers were exposed to, carbon disulfide and carbon tetrachloride, had the strongest association with leukemia. There was no association between exposure to carbon disulfide and any other cancer. Wilcosky et. al. (1984) however, suggests "cautious interpretation" due to the large number of variables and that the interpretation of this apparent association between carbon disulfide and leukemia is unclear. In contradiction to these studies, Nurimen and Hernberg (1984) found no association between occupational exposure to carbon disulfide and cancer mortality in a 15-year prospective follow-up study on viscose rayon workers.

Ecotoxicity

No data regarding the toxicity of carbon disulfide to aquatic or terrestrial life, domestic or wild, were found in the literature reviewed.

Standards, Criteria and Guidelines

Unclassified by EPA as to carcinogenicity.

Oral Slope Factor:	NA
Chronic Oral RfD:	1.0×10^{-1} mg/kg/day
Subchronic Oral RfD:	1.0×10^{-1} mg/kg/day
MCL:	NA

BIBLIOGRAPHY

Atkinson, R. et. al., Rate Constants for the Reaction of Hydroxyl Radicals with Carbonyl Sulfide, Carbon Disulfide and Dimethyl Thither Over the Temperature Range 299-430°K, *Chem. Phys, Lett.* 54: 14-18, 1978, (Cited in HEEP, 1986).

Beliles, R.P. et. al., *Teratogenic-Mutagenic Risk of Workplace Contaminants: Trichloroethylene, Perchloroethylene and Carbon Disulfide*, Prepared by Litton Bionetics, Inc., under contract number 210-77-0047, NIOSH, Washington, D.C., 1980, (Cited in HEEP, 1986).

Berg, G.L., *1981 Farm Chemical Handbook*, Mister Publishing Co., Willoughby, OH, p. C-62 - C-63, 1981, (Cited in HEEP, 1986).

Bergman, K. et. al., Tissue Disposition of Carbon Disulfide: I. Whole-Body Autoradiography of ^{35}S- and ^{14}C- Labeled Carbon Disulfide in Adult Male Mice, *Acta Pharmacol. Toxicol.* 54(2): 141-150, 1984, (Cited in HEEP, 1986).

Bremner, J.M., and W.L. Banwait, Sorption of Sulfur Gases by Soils, *Soil Biol. Biochem.* 8:79-83, 1976, (Cited in HEEP, 1986).

Checkoway, H. et. al., An evaluation of the associations of leukemia and rubber industry solvent exposures, *Am. J. Ind. Med.*, 5(3): 239-249, 1984.

CMR (Chemical Marketing Reporter), *Chemical Profile: Carbon Disulfide*, January 24, 1083, (Cited in HEEP, 1986).

Donner, M. et. al., Carbon Disulfide is not Mutagenic in Bacteria or Drosophila, *Mutat. Res.* 91(3): 163-166 1981, (Cited in HEEP, 1986).

Gondzik, M., Effect of carbon disulfide on testicles and kidneys, *Med. Pr.*, 27(1): 21, 1976.

Hedenstet, A. et. al., Mutagenicity and Metabolism Studies on 12 Thorium and Dithiocarbamate Compounds Used as Accelerators in the Swedish Rubber Industry, *Mutat. Res.* 68: 313-325, 1979.

Jones-Price, C. et. al., Teratologic evaluation of carbon disulfide (CAS No. 75-15-0) administered to CD rats on gestational days 6 through 15. *Gov. Rep. Announce. Index (U.S.)*, 84(15)80, FDA/NCTR-84/78, 1984a.

McKenna, K.J. and V. DiStefano, Carbon Disulfide I., The Metabolism of Inhaled Carbon Disulfide in the Rat, *J. Pharmacol, Exp. Ther.* 202(2): 245-252, 1977, (Cited in HEEP, 1986).

Nurimen, M. and S. Hernberg, Cancer mortality among carbon disulfide exposed workers, *J. Occ. Med.*, 26(5): 341, 1984.

Peyton, T.O. et al., *Carbon Disulfide, Carbonyl Sulfide, Literature Review and Environmental Assessment,* ORD, U.S., EPA, Washington, D.C., EPA 600/9-78-009, 1978, (Cited in HEEP, 1986)

Pilarski, K. et. al., Effect of carbon disulfide on the hematopoietic system of rats, I, Evaluation of peripheral blood, *Acta Haematol. Pol.*, 4(1): 33, 1973.

Timmerman, R.W., *Carbon Disulfide In: Kirk-Othmer Encyclopedia of Chemical Technology, Vol. 4, 3rd ed.,* M. Grayson and D. Eckroth, Ed., John Wiley and Sons, Inc., New York, p. 742-757, 1978, (Cited in HEEP, 1986)

U.S. EPA, *Drinking Water Regulations and Health Advisories.*

U.S. EPA, *Health and Environmental Effects Profile for Carbon Disulfide*, EPA/600/X-86/155, June, 1986.

U.S. EPA, *Integrated Risk Information System (IRIS).*

U.S. EPA, *Health Effects Assessment Summary Tables (HEAST).* FY1991.

U.S. EPA, OERR. *CERCLA Compliance with Other Laws Manual Interim Final.* August, 1988.

U.S. EPA, *Oil and Hazardous Materials Technical Assistance Data System*, On line, 1985, (Cited in HEEP, 1986).

Vigliani, E.C., Carbon disulfide poisoning in viscose rayon factories, *Br. J. Ind. Med.*, 11:235-244, 1954.

Wilcosky, T.C. et. al., Cancer mortality and solvent exposures in the rubber industry, *Am. Id. Hyg. Assoc. J.*, 45(12): 809-811, 1984.

Windholz, M., Ed, *The Merck Index*, 10th ed., Merck and Co., Rahway, NJ, p. 1,796, 1983, (Cited in HEEP, 1986).

Wood, W.P. and J. Heicklan, *The Photooxidation of Carbon Disulfide*, J. Phys. Chem., 75: 854-860, 1971, (Cited in HEEP, 1986).

CARBON TETRACHLORIDE

Use: Carbon Tetrachloride (CCl_4) is used as a solvent for oils, fats, lacquers, varnishes, rubber, waxes, and resins. Fluorocarbons are chemically synthesized from CCl_4. It is also used as an azeotropic drying agent for spark plugs, a dry-cleaning agent, a fire-extinguishing agent, a fumigant, and an anthelmintic agent (Sittig, 1991).

Chemical and Physical Properties

Chemical Formula:	CCl_4		
MW:	153.8	MP:	-23°C
VP:	91.3 mm Hz at 20°C	BP:	76.5°C
Sol. (water):	785 mg/l at 20°C		
Sol. (organics):	miscible		

Fate and Transport

ATSDR (1989) reports that nearly all CCl_4 released to the environment exists in the atmosphere. Galbally (1976) reports that, although CCl_4 is moderately soluble in water, only about 1% of the CCl_4 present in the environment exists dissolved in surface waters and oceans. This is due to the relatively high rate of volatilization experienced by low molecular weight chlorinated hydrocarbons (Dilling et al., 1975; Dilling, 1977). Hansch and Leo (1979) report that, based on its octanol:water partition coefficient, CCl_4 tends to be adsorbed to organic matter in soils. Studies by McConnell et al. (1975) and Briggs (1973) suggest that CCl_4 is adsorbed by organic matter in sediments.

ATSDR (1989) reports on several studies which state that CCl_4 is very stable in the troposphere, primarily because CCl_4 does not react with hydroxyl radicals that initiate breakdown and transformation reactions of other volatile hydrocarbons. Davis et al. (1975) report that CCl_4 does not photodissociate in the troposphere since, in the vapor state, CCl_4 has no chromophores which absorb light in the visible or near ultraviolet regions of the electromagnetic spectrum which prevail in the troposphere. The rate of oxidation of CCl_4 is so slow that the tropospheric half-life of CCl_4 is greater than 330 years (Cox et al., 1976). Carbon tetrachloride that is not removed from the troposphere by rainfall migrates upward into the stratosphere, where it may be photodegraded by shorter ultraviolet light more prevalent at this level, to form the CCl_3 radical and chlorine atoms (Molina and Rowland, 1974; Pearson and McConnell, 1975). Molina and Rowland (1974) report that the rate of photodissociation begins to become important at altitudes of 20 km or higher, and increases with altitude. Atmospheric half-life estimates range from 30 to 100 years (Molina and Rowland, 1974; Simmonds et al., 1973). ATSDR (1989) reports that chlorine atoms and other chlorine species formed by photodecomposition of CCl_4 in the stratosphere can catalyze reactions that destroy ozone. NAS (1984) estimates that, at steady-state, a 1% decrease in the ozone layer occurs due to the release of CCl_4 and other volatile halocarbons.

In aquatic media, ATSDR reports that CCl_4 does not photodegrade or oxidize to any appreciable extent. Mabey and Mill (1978) estimated the half-life for hydrolysis of 1 ppm

CCl_4 to be 7,000 years. In the ocean, hydrolysis may be the cause of decreasing CCl_4 concentrations with depth (Lovelock et al., 1973). Pearson and McConnell (1975) and Neeley et al. (1974) report that although CCl_4 is relatively lipophilic, there is little tendency for this compound to bioaccumulate in aquatic or marine organisms.

Pharmacokinetics

Lehmen and Schmidt-Kehl (1936) estimate that absorption of CCl_4 across the lung by human is about 60%. Orally, animal studies indicate that 80 to 85% of a dose may be recovered in expired air, indicating that gastrointestinal absorption is at least 85% (Marchand et al., 1970; Paul and Rubinstein, 1963). Kim et al. (1988) reports that the use of corn oil as the vehicle for administering CCl_4 slows and diminishes absorption. ATSDR (1989) reports that CCl_4 is absorbed through the skin of humans, though much less readily than from the lung. McCollister et al. (1951) reports that absorption of CCl_4 vapors through the skin is minimal. ATSDR (1989) reports that CCl_4 is distributed according to the rate of blood perfusion and the lipid content of tissues. Therefore, the highest concentrations of CCl_4 occur in fat, bone marrow, liver, brain, and kidney. ATSDR (1989) reports that the major metabolic products of CCl_4 include phosgene, trichloromethane, hexachloroethane, carbon monoxide, and carbon dioxide. The metabolic pathway for CCl_4 is a saturable or self-destructing system (ATSDR, 1989). ATSDR (1989) also reports that the metabolism of CCl_4 is an integral step in the pathway of this compound's toxicity. The detailed mechanism linking metabolism to toxicity, however, is not yet clear. Studies in animals indicate that about 30 to 40% of an inhaled dose of CCl_4 is excreted in expired air and about 50 to 60% is excreted in feces (McCollister et al., 1951; Paustenbach et al., 1986). ATSDR (1989) reports that relatively little of inhaled CCl_4 is excreted in the urine. The majority of the expired product is parent CCl_4, with small amounts of CO_2 (ATSDR, 1989). Orally, at doses of 50 mg/kg or higher, most of the dose (70 to 90%) was recovered as expired CCl_4, with lesser amounts of expired CO_2 or $CHCl_3$ and nonvolatile metabolites in feces or urine. Volunteers who immersed their thumbs in liquid CCl_4 rapidly excreted the compound in expired air (Stewart and Dodd, 1964).

Human Toxicity

Noncarcinogenic Effects

Systemic Effects

Bruckner et al. (1986) exposed male Sprague-Dawley rats to 1, 10, or 33 mg/kg/day CCl_4 by corn oil gavage, 5 days/week for 12 weeks. Liver lesions were evidenced by mild centrilobular vacuolization and statistically significant increases in serum sorbitol dehydrogenase activity. ATSDR (1989) reports that many human fatalities have occurred as the result of CCl_4 exposure by ingestion or inhalation. Nearly all fatal cases involve individuals with a history of alcohol consumption with non-drinkers being considerably less susceptible. The lowest inhalation exposure reported to cause death was 250 ppm for 15 minutes (Norwood et al., 1950). Minimum oral doses of 40 to 320 mg/kg have been reported to cause death as well (Lamson et al., 1928; Umiker and Pearce, 1953; Von Oettingen, 1964). ATSDR (1989) reports that CCl_4 exposure can result in a variety of

neurological effects including dyspepsia (nausea, vomiting, abdominal pain), headache, vertigo, confusion, lethargy, and stupor. Hepatotoxicity evidenced by clinical signs such as jaundice or swollen and tender liver, biochemical alterations, or histological examination, has been observed in nearly every study of CCl_4 exposure (ATSDR, 1989). Injury to the kidney is also observed in nearly every study of human exposure to CCl_4 (ATSDR, 1989). Several studies have determined a number of tissues other than the liver, kidney, and CNS that are affected by CCl_4 exposure: the adrenals, pancreas, testes, pituitary, spleen, and thyroid.

Teratogenic and Other Developmental Effects

ATSDR (1989) reports on several studies of the developmental effects of CCl_4 exposure via inhalation and ingestion. No indications of developmental toxicity were observed. Reproductively, rats exposed to CCl_4 for three generations exhibited decreased fertility at doses of 200 ppm or higher (Smyth et al., 1936). At the same doses, Adams et al. (1952) observed marked degeneration of testicular germinal epithelium in rats. Significant reproductive effects following oral exposure have not been observed (Alumot et al., 1976).

Mutagenic Effects

Carbon tetrachloride was not mutagenic to either *S. typhimurium or E. coli* (McCann et al., 1975; Simmon et al., 1977; Uehleke et al., 1976). At low concentrations, carbon tetrachloride did not produce chromatic or chromosomal aberrations in an epithelial cell line derived from rat liver (Dean and Hodson-Walker, 1979). In vivo unscheduled DNA synthesis assays in male Fischer 344 rats have also been negative (Mirsalis and Butterworth, 1980; Mirsalis et al., 1982). CCl_4 produced mitotic recombination and gene conversion in S. cerevisiae, but only at concentrations which reduced viability to 10% (Callen et al., 1980). EPA (IRIS) reports that CCl_4 may be metabolized to reactive intermediates capable of binding to cellular nucleophilic macromolecules. Negative responses in bacterial mutagenicity assays may have been due to inadequate metabolic activation in the test systems (IRIS).

Carcinogenic Effects

NCI (1976a,b; 1977) administered CCl_4 in corn oil by gavage at doses of 47 and 94 mg/kg/dose for males and 80 and 159 mg/kg/dose for females, 5 times/week, for 78 weeks. The incidence of hepatocellular carcinoma was increased in comparison to unexposed animals. In this same study, B6C3F1 mice received doses of 1250 and 2500 mg/kg CCl_4. A significant increase in the incidence of hepatocellular carcinoma was observed. Edwards et al. (1942) exposed 56 male and 19 female L mice, which have a low incidence of spontaneous hepatomas, to 0.1 ml of 40% CCl_4 2 to 3 times/week over 4 months for a total of 46 treatments. The combined hepatoma incidence of treated mice was 47% for males and 38% for females. Della Porta et al. (1961) exposed Syrian golden hamsters (10/sex/dose) to CCl_4 by gavage, weekly, for 30 weeks. For the first 7 weeks, 0.25 ml of 0.05% CCl_4 in corn oil was administered; this dose was halved for the remaining 23 weeks. All the hamsters were observed for an additional 25 weeks. All of the hamsters that were killed or dying during weeks 43 to 55 had liver cell carcinomas, compared with zero in controls.

Ecotoxicity

Data indicate that the acute toxicity of CCl_4 for freshwater aquatic life and saltwater aquatic life occurs at concentrations as low as 35,200 µg/L and 50,000 µg/L, respectively. No acute or chronic effects have been observed at concentrations lower than 3400 µg/L. The bluegill has been found to bioconcentrate CCl_4 by a factor of 30 within 21 days. The biological half life in the tissues was less than one day. Therefore tissue residues of CCl_4 should not pose a potential hazard to aquatic life (EPA, 1980).

Standards, Criteria, and Guidelines

EPA Class B2 Carcinogen

Oral Slope Factor:	1.3×10^{-1} $(mg/kg/day)^{-1}$	
Inhal. Slope Factor:	5.2×10^{-2} $(mg/kg/day)^{-1}$	
Inhal. Unit Risk:	1.50E-05 $(\mu g/m^3)^{-1}$	
Chronic Oral RfD:	7.0×10^{-4} mg/kg/day	
Chronic Inhal. RfD:	NA	
RFC:	2.00E-03 mg/m^3	
Subchronic Oral RfD:	7.0×10^{-3} mg/kg/day	
Subchronic Inhal, RfD:	NA	
MCL:	5 µg/l	
AWQC:	Water and Fish Consumption:	0.25 µg/l
	Fish Consumption:	4.5 µg/l

BIBLIOGRAPHY

Adams, E.M., Spencer, H.C., Rowe, V.K., et al. 1952. Vapor toxicity of carbon tetrachloride determined by experiments on laboratory animals. *Arch. Ind. Hyg. Occup. Med.* 6:50-66.

Alumot, E., Nachtomi, E., Mandel, E., et al. 1976. Tolerance and acceptable daily intake of chlorinated fumigants in the rat diet. *Food Cosmet. Toxicol.* 14:105-110.

ATSDR, 1989. *Toxicological Profile for Carbon Tetrachloride.*

Briggs, G.G. 1973. A simple relationship between soil adsorption of organic chemicals and their octanol/water partition coefficients. *Proc. 7th Br. Insec. Fung. Conf. (1973).* 83-86.

Bruckner, J.V., McKenzie, W.F., Muralidhara, S., Luthra, R., Kyle, G.M., and Acosta, D. 1986. Oral toxicity of carbon tetrachloride: Acute, subacute and subchronic studies in rats. *Fund. Appl. Toxicol.* 6(1):16-34.

Callen, D.F., Wolf, C.R., and Philpot, R.M. 1980. Cytochrome P-450 mediated genetic activity and cytoxicity of seven halogenated aliphatic hydrocarbons in Saccharomyces cerevisiae. *Mutat. Res.* 77:55-63.

Cox, R.A. et al. 1976. Photochemical oxidation of halocarbons in the troposphere. *Atmos. Environ.* 10:305-308 (cited in ATSDR).

Davis, D.D. et al. 1975. Effect of wavelength in the gas-phase photolysis of carbon tetrachloride at 253.7, 184.9, 147, and 106.7 nm. *J. Phys. Chem.* 79:11-17 (cited in ATSDR).

Dean, B.J. and Hodson-Walker, G. 1979. An in vitro chromosome assay using cultured rat-liver cells. *Mutat. Res.* 64:329-337.

Della Porta, G., Terracini, B., and Shubik, P. 1961. Induction with carbon tetrachloride of liver cell carcinomas in hamsters. *J. Natl. Cancer Inst.* 26(4):855-863.

Dilling, W.L. et al. 1975. Evaporation rates and reactivities of methylene chloride, chloroform, 1,1,1-trichloroethane, trichloroethylene, tetrachloroethylene, and other chlorinated compounds in aqueous solutions. *Environ. Sci. Technol.* 9:833-838 (cited in ATSDR).

Dilling, W.L. 1977. Interphase transfer processes. II. Evaporation of chloromethanes, ethanes, propanes, and polypropylenes from dilute aqueous solutions. Comparisons with theoretical predictions. *Environ. Sci. Technol.* 11:405-409 (cited in ATSDR).

Edwards, J.E. and Dalton, H.A. 1942. Induction of cirrhosis of the liver and of hepatomas in mice with carbon tetrachloride. *J. Natl. Cancer Inst.* 3:19-41.

Edwards, J.E., Heston, W.E., and Dalton, H.A. 1942. Induction of the carbon tetrachloride hepatoma in strain L. mice. *J. Natl. Cancer Inst.* 3:297-301.

Galbally, I.E. 1976. Man-made carbon tetrachloride in the atmosphere. *Science* 193:573-576

Hansch, C. and Leo, A. 1979. Substituent constants for correlation analysis. In: *Chemistry and Biology*. New York, NY. John Wiley and Sons (cited in ATSDR).

Kim, H.J., Gallo, J.M., Bruckner, J.V. 1988. Effect of dosing vehicles on the pharmacokinetics of orally administered carbon tetrachloride in rats. (Submitted for publication to *Toxicol. Appl. Pharmacol.*)

Lamson, P.D., Minot, A.S., Robbins, B.H. 1928. The prevention and treatment of carbon tetrachloride intoxication. *J. Am Med. Assoc.* 90:345-346.

Lehmann, K.B. and Schmidt-Kehl, L. 1936. The thirteen most important chlorinated aliphatic hydrocarbons from the standpoint of industrial hygiene. *Arch. Hyg.* 116:132-200 (cited in ATSDR).

Lovelock, J.E. 1973. Halogenated hydrocarbons in and over the Atlantic. *Nature* 241:194-196 (cited in ATSDR).

Mabey, W. and MIll, T. 1978. Critical review of hydrolysis of organic compounds in water under environmental conditions. *J. Phys. Chem. Ref. Data* 7:383-415 (cited in ATSDR).

Marchand, C., McLean, S., Plaa, G.L. 1970. The effect of SKF 525A on the distribution of carbon tetrachloride in rats. *J. Pharmacol. Exp. Therap.* 714:232-238.

McCann, J. Choi, E., Yamasaki, E., and Ames, B.N. 1975. Detection of carcinogens as mutagens in the Salmonella/microsome test: Assay of 300 chemicals. *Proc. Natl. Acad. Sci.* 72:5153-5139.

McCollister, D.D., Beamer, W.H., Atchison, G.J. et al. 1951. The absorption, distribution and elimination of radioactive carbon tetrachloride by monkeys upon exposure to low vapor concentrations. *J. Pharmacol. Exp. Therap.* 102:112-124.

McConnell, G. et al. 1975. Chlorinated hydrocrabons and the environment. *Endeavor* 34:13-18 (cited in ATSDR).

Mirsalis, J.C. and Butterworth, B.E. 1980. Detection of unscheduled DNA synthesis in hepatocyte isolated from rats treated with genotoxic agents: An in vivo-in vitro assay for potential carcinogens and mutagens. *Carcinogenesis* 1:621-625.

Mirsalis, J.C., Tyson, C.K., and Butterworth, B.E. 1982. Detection of genotoxic carcinogens in the in vivo-in vitro hepatocyte DNA repair assay. *Environ. Mutagen.* 4: 553-562.

Molina, M.J. and Rowland, F.S. 1974. Predicted present stratospheric abundances of chlorine species from photodissociation of carbon tetrachloride. *Geophys. Res. Lett.* 1:309-312 (cited in ATSDR).

NAS, 1984. *Causes and Effects of Changes in Stratospheric Ozone: Update 1983.* Washington, DC: National Academy of Sciences (cited in ATSDR).

NCI (National Cancer Institute). 1976b. Carcinogenesis Bioassay of Trichloroethylene. *National Cancer Institute Carcinogenesis Technical Report Series, No. 2.* NCI-CG-TR-2. February.

NCI (National Cancer Institute). 1977. Bioassay of 1,1,1-Trichloroethane for Possible Carcinogenicity. *National Cancer Institute Carcinogenesis Technical Report Series, No. 3.* NCI-CG-TR-3. January.

Neeley, B.W. et al. 1974. Partition coefficient to measure bioconcentrations potential of organic chemicals in fish. *Environ. Sci. Technol.* 8:1113 (cited in ATSDR).

Norwood, W.D., Fuqua, P.A., Scudder, B.C. 1950. Carbon tetrachloride poisoning. Anch. *Ind. Hyg. Occup. Med.* 1:90-100.

Paul, B.B. and Rubinstein, D. 1963. Metabolism of carbon tetrachloride and chloroform by the rat. *J. Pharmacol. Exper. Therap.* 141:141-148.

Paustenbach, D.J., Carlson, G.P., Christian, J.E., et al. 1986a. A comparative study of the pharmacokinetics of carbon tetrachloride in the rat following repeated inhalation exposures of 8 and 11.5 hr/day. *Fund. Appl. Toxicol.* 6:484-497.

Paustenbach, D.J., Christian, J.E., Carlson, G.P., et al. 1986b. The effect of an 11.5-hr/day exposure schedule on the distribution and toxicity of inhaled carbon tetrachloride in the rat. *Fund. Appl. Toxicol.* 6:472-483.

Pearson, C.R. and McConnell, G. 1975. Chlorinated C1 and C2 hydrocarbons in the marine environment. *Proc. P. Soc. Lond. B.* 189:305-332 (cited in ATSDR).

Simmon, V.F., Kauhanen, K., and Tardiff, R.G. 1977. Mutagenic activity of chemicals identified in drinking water. In: *Progress in Genetic Toxicology.* D. Scott, B.A. Bridges, and F.H. Sobels, ed. Elsevier/North-Holland Biomedical Press, New York. p. 249-258.

Simmonds, P.G. et al. 1983. The atmospheric lifetime experiment. 6. Results from carbon tetrachloride based on three years data. *J. Geophys. Res.* 88:8427-8441 (cited in ATSDR).

Sittig, M. 1991. *Handbook of Toxic and Hazardous Chemicals and Carcinogens* (cited in ATSDR).

Smyth, H.F., Smyth, H.F., Jr., Carpenter, C.P. 1936. The chronic toxicity of carbon tetrachloride; animal exposure and field studies. *J. Ind. Hyg. Toxicol.* 18:277-298.

Stewart, R.D. and Dodd, H.C. 1964. Absorption of carbon tetrachloride, trichloroethylene, tetrachloroethylene, methylene chloride and 1,1,1-trichloroethane through the human skin. *Am. Ind. Hyg. Assoc. J.* 25:439-446.

Stewart, R.D., Dodd, H.C., Erley, D.S., et al. 1965. Diagnosis of solvent poisoning. *J. Am. Med. Assoc.* 193:115-118.

Uehleke, H., Greim, H., Kramer, M., and Werner, T. 1976. Covalent binding of haloalkanes to liver constituents, but absence of mutagenicity on bacteria in a metabolizing test system mutation. *Research* 38:114.

Umiker, W. and Pearce, J. 1953. nature and genesis of pulmonary alternations in carbon tetrachloride poisoning. *Arch. Pathol.* 55:203-217.

U.S. EPA, 1980. Ambient Water Quality Criteria for Carbon Tetrachloride.

von Oettingen, W.F. 1964. The halogenated hydrocarbons of industrial and toxicological importance. In: Browning, E., ed. *Elsevier Monographs on Toxic Agents.* New York, NY: Elsevier Publishing Co.

CHLOROBENZENE

Use

Chlorobenzene is a colorless liquid with a mild aromatic odor. It is used in the manufacture of aniline, phenol, and chloronitrobenzene as well as being produced as an intermediate in the manufacture of dye-stuffs and many pesticides (Sittig, 1991).

Chemical and Physical Properties

MF: C_6H_5Cl BP: 131-132°
MP: -45°C
MW: 112.56 FP: 28°C
Sol. (water): insoluble
Sol. (organics): soluble in alcohol, benzene, chloroform, ether

Fate and Transport

The U.S. EPA (1987) reports that chlorobenzene released to the atmosphere is expected to degrade slowly by free radical oxidation. Due to its volatility and insolubility, chlorobenzene in water is expected to partition rapidly to the air. In soils, chlorobenzene will most likely bind to soil and migrate slowly to ground water, resisting biodegradation (U.S. EPA, 1987). Chlorobenzene has been shown to bioaccumulate in fish, aquatic invertebrates, and algae, and in higher organisms it has been shown to be metabolized to other compounds (U.S. EPA, 1987).

Pharmacokinetics

The U.S. EPA (1987) reports that, based upon the high lipid solubility of chlorobenzene along with the absorption characteristics of benzene and the smaller chlorinated hydrocarbons that are also highly lipid soluble, the EPA will assume that 100 percent of an orally administered dose and 60 percent of an inhaled dose are absorbed over a period of one to several hours and that the dose is retained.

Sullivan et al. (1983) found that male Sprague-Dawley rats exposed to 100, 400, or 700 ppm ^{14}C-chlorobenzene acutely or over an 8-hour period by inhalation exhibited the highest concentration in adipose tissue. The kidney and the liver also showed significant accumulation. The data suggest a preferential distribution of chlorobenzene to the adipose tissue at all dose levels while it seems to be proportionally distributed to the kidney and liver with dose. Additionally, multiply-exposed rats (over 8 hours) tended to exhibit higher tissue burdens than rats exposed only once.

The U.S. EPA (1987) states that, upon termination of exposure, chlorobenzene would be expected to be released from the adipose tissue and become available for metabolic activation and potential continuation of induction of toxicity.

Williams et al. (1975) reported that the principal metabolites of chlorobenzene administered to mammals, including humans, are p-chlorophenol, p-chloroatechol, and p-chlorophenyl-mercapturic acid.

Spencer and Williams (1950) and Azouz et al. (1953) report that the chlorophenol metabolite is excreted as the ethereal sulfate or the gluconide. Williams et al. (1975) and Sullivan et al. (1983) report other excretion products to be chlorophenyl mercapturic acid, 4-chlorocatechol, and to a lesser degree in some species; phenol and hydroquinone.

In rats exposed to 100 ppm in air for eight hours, 5 percent was excreted via inhalation and 95 percent in the urine (Sullivan et al., 1983). At 700 ppm, 32 percent was exhaled and 68 percent excreted in the urine. The authors concluded that increasing amounts of the chemical are exhaled unchanged as the metabolic pathways for biotransformation become saturated.

Human Toxicity

Noncarcinogenic

Systemic Effects

In a study by the Monsanto Co. (1967a), male and female beagle dogs were given chlorobenzene orally by capsule at doses of 27.25, 54.5, or 272.5 mg/kg/day, 5 days/week, for 13 weeks. At 54.5 mg/kg/day slight bile duct proliferation, cytologic alternations and leukocytic infiltration of the stroma in liver occurred. The highest dose of 272.5 mg/kg/day resulted in death; body weight loss; hematologic changes; and pathologic changes in the liver which included bile duct hyperplasia, cytologic changes, leukocytic infiltration, and centrolobular degeneration; kidney changes; gastrointestinal mucosa changes; changes to hematopoietic tissue; and alterations in clinical chemistry and urine analysis.

The NTP (1985) conducted a 13-week range-finding study in groups of five male and five female rats and mice with chlorobenzene administered by gavage. Both species were administered 0, 60, 125, 250, 500 or 750 mg/kg/day, 5 days/week. 100 percent lethality occurred in male mice treated with 500 mg/kg or 750 mg/kg within one week. Death was accompanied by histopathological lesions in many organs. All female mice in the 750 mg/kg group died by week 10. At 250 mg/kg a 50 percent reduction in body weight gain and histopathological lesions were observed. Male mice at the 125 mg/kg dose exhibited increased liver weights and one male in this group and one male in the low dose group exhibited liver necrosis. In rats, the highest doses (500, 750 mg/kg) resulted in decreased body weight gain and histopathological alterations in both sexes. The females exhibited altered serum biochemistries. Decreased survival was observed in the highest dose group. AT 250 mg/kg the only observed adverse effect was minimal centrobular hepatocellular necrosis.

Most of the inhalation studies evaluated by the U.S. EPA (1987) reported no adverse effects or minimal effects.

Teratogenic and Other Developmental Effects

John et al. (1984) and Hayes et al. (1982) exposed pregnant rats and rabbits to 0, 75, 210, or 590 ppm chlorobenzene via inhalation for 6 hours/day during the period of major organogenesis (days 6-15 for rats, 6-18 for rabbits). Decreased body weight gain was observed in rats at the highest dose. No teratological effects were observed in rat fetuses at any dose level. Rabbits exhibited increased liver weights (relative and absolute) at the mid and high dose. No structural malformations were observed in rabbit fetuses either.

Mutagenic Effects

Chlorobenzene was not mutagenic for *Salmonella typhimurium* TA 98, TA100, TA1535, TA1537, TA1538; with or without addition of rat liver or hamster liver homogenate (duPont, 1977; Lawlor et al., 1979; Merck, 1978; Monsanto, 1976a; NTP, 1982; Simmon et al., 1979). Lawlor et al. (1979) and Simmons et al. (1979) report that chlorobenzene does not induce DNA damage in *E. coli* strains WP2 uvr A+rec+ or WP100 uvr A-rec- or *S. typhimurium* strains TA1978 uvr B+ or TA1538 uvr 8-. Additionally, it did not induce specific locus forward mutations in mouse lymphoma L5178Y cells, either with or without metabolic activation (Monsanto, 1976b).

Chlorobenzene did, however, cause increases in the number of revertants in *Actinomycetes antibioticus-400* (Keskinova, 1968) and *Asperigillus nidulans* (Prasad, 1970; Prasad and Promer, 1968), and mitotic disturbances in *Allium cepa* (Ostergen and Levan, 1943). The chemical also included reciprocal recombination in *Saccharomyces cerevasiae* strain D3 with metabolic activation (Simmon et al, 1979).

Carcinogenic Effects

In a gavage study of rats and mice exposed to between 30 and 120 mg/kg/day, 5 days/week for 103 weeks no statistically significant increase in the frequency of carcinomas of any type were observed (NTP, 1985).
No other data regarding the carcinogenicity of chlorobenzene were found in the literature reviewed.

Ecotoxicity

ICF (1985) reports that chlorobenzene was acutely toxic to fish at levels greater than 25 mg/liter and to aquatic invertebrates at levels greater than 10 mg/liter. ICF (1985) also stated that chlorobenzene was shown to have a bioaccumulation factor of about 1,000 in fresh water species.

No data regarding the ecotoxicity of chlorobenzene to terrestrial life, wild or domestic, were found in the literature reviewed.

Standards, Criteria and Guidelines

EPA Class D Carcinogen

Oral Slope Factor:	NA
Chronic Oral RfD:	2.0×10^{-2} mg/kg/day
Subchronic Oral RfD:	2.0×10^{-2} mg/kg/day
MCL:	NA

BIBLIOGRAPHY

Azouz, W.M. et al., Studies in detoxication. 51: The determination of catechols in urine, and the formation of catechols in rabbits receiving halogenobenzenes and other compounds, dihydroxylation *in vivo. Biochem. J.* 55(1):146-151. 1953. (Cited in HA, 1987).

Dilley, J.V. Toxic evaluation of inhaled chlorobenzene. NIOSH, DHEW, Cincinnati, OH. Contract 210-76-0126. (Cited in HEAST).

E.I. duPont DeNemours and Col, *Mutagenic activity of monochlorabenzene in the salmonella-microsome assay.* Haskell Laboratory for Toxicology and Industrial Medicine. Unpublished report. 1977. (Cited in IRIS).

Hayes, W.C. et al., *Monochlorobenzene inhalation teratology study in rats and rabbits.* Unpublished report. Toxicology Research Laboratory. Dow Chemical Company. 115 pp. 1981. (Cited in HA, 1987).

ICF Clements Assoc., *Chemical, Physical, and Biological Properties of Compounds Present at Hazardous Waste Sites,* 1985.

John, J.A. et al., Inhalation teratology study on monochlorobenzene in rats and rabbits. *Toxicol. Appl. Pharmacol.* 76:365-373. 1984. (Cited in HA, 1987).

Keskinova, D.V., The effect of dimethylcyclodiazomethane in chlorobenzene solution on the process of mutagenesis in *Actinomyces antibioticus-400. Genetika.* 4(8):121-125. 1968. (Cited in IRIS).

Lawlor, T. et al., Evaluation of the genetic activity of nine chlorinated phenols, seven chlorinated benzenes, and three chlorinated hexanes. *Environ. Mutagen.* 1:143 (abstract). 1979. (Cited in IRIS).

Merck and Co., *Summary of monochlorobenzene bacterial mutagen test (Ames test).* Office of Pesticide and Toxic Substances, U.S. EPA, Wash. D.C. TSCA Sec. 8(d) submission 8DHQ-1078-0302. 1978. (Cited in IRIS).

Monsanto Company, *13-week oral administration--dogs. Monochlorobenzene.* Final Report. Prepared by Hazelton Laboratories, Project No. 241-105, Feb. 24, 1967. (Cited in IRIS).

Monsanto Co., *Mutagenicity evaluation of B10-76-86-CP-5535 (WGK).* Final Report. LBI Project No. 2457. Litton Bionetics, Kensington, MD. Unpublished. 1976a. (Cited in IRIS).

Monsanto Co., *Mutagenicity evaluation of B10-76-86-CP-5535 (LOX).* Final Report. LBI Project No. 2457. Litton Bionetics, Kensington, MD. Unpublished. 1976b. (Cited in IRIS).

NTP (National Toxicology Program), *Carcinogenesis studies of chlorobenzene (CAS No. 108-99-7) in F344/N rats and B6C3F1 mice (gavage studies).* NTP-82-90. NIH Publ. No. 83-2517. 1985. (Cited in HEA, 1984 and IRIS).

NTP (National Toxicology Program), *Environmental Mutagen Test Development Program,* Research Triangle Park, NC. 1978. (Cited in IRIS).

Ostergen, G. and A. Levin, The connection between c-mitotic activity and water solubility in some monocyclic compounds. *Hereditas* 29:496-498. 1943. (Cited in IRIS).

Prasad, I., Mutagenic effects of the herbicide 3,4-dichlororopion anilide and its degradation products. *Can. J. Biochem.* 16:369-372. 1970. (Cited in IRIS).

Prasad, I. and D. Pramer, Mutagenic activity of some chloroanilines and chlorobenzenes. *Genetics.* 60:212-213. 1968. (Cited in IRIS).

Simmon, V.F. et al., *In vitro microbiological genotoxicity tests of chlorobenzene, m-dichlorobenzene, o-dichlorobenzene, and p-dichlorobenzene.* Final Report. SRI International, Menlo Park, CA. Unpublished. 1979. (Cited in IRIS).

Sittig, M., *Handbook of Toxic and Hazardous Chemicals,* 1991.

Spencer, B. and R.T. Williams, Studies in detoxication. 33. The metabolism of halogenobenzenes. A comparison of the glucuronic acid, etheral sulfate and mercapturic acid. Conjugation of chloro-, bromo-, and iodobenzene and of the o-, m-, and p-chlorophenyl glucuronides. *Biochem. J.* 47:279-284. 1950. (Cited in HA, 1987).

Sullivan, T.M. et al., The pharmacokinetics of inhaled chlorobenzene in the rat. *Toxicol. Appl. Pharmacol.* 71:194-203. 1983. (Cited in HA, 1987).

U.S. EPA, *Drinking Water Regulations and Health Advisories.*

U.S. EPA, Office of Drinking Water, *Health Advisory for chlorobenzene (HA),* 1987.

U.S. EPA, *Health Effects Assessment for chlorobenzene (HEA),* 1984.

U.S. EPA, *Integrated Risk Information System (IRIS).*

U.S. EPA, *Health Effects Assessment Summary Tables (HEAST).*

U.S. EPA, OERR. *CERCLA Compliance with Other Laws Manual Interim Final.* August, 1988.

Williams, R.T. et al., Species variation in the metabolism of some organic halogen compounds. In: *Ecological Toxicological Research.* A.D. McIntrye and C.F. Mills, Ects. Plenum Press, New York, NY, p. 99-105. 1975. (Cited in HA, 1987).

CHLOROFORM

Use

Chloroform was first used in the medical field as an anesthetic and as an inhalant for asthmatics. Because of its toxic effects, chloroform's use was eventually abandoned in medicine (Sittig, 1991). It is presently used in the production of chlorofluorocarbons, as a solvent, and in the extraction of vitamins, penicillin, and other antibiotics. Chloroform is often produced during the chlorination of public drinking water. As a result, a large percentage of the population is exposed daily to small quantities of chloroform (IARC, 1979).

Chloroform is also used as an insecticidal fumigant, in the manufacture of artificial silks and plastics, and as a residual additive in a number or drugs (IARC, 1979).

Chemical and Physical Properties

Chemical Formula: $CHCl_3$

MW:	119.38	BP:	61.7°C
SG:	1.483 at 20°C	MPP:	-63.5°C
FP:	>140°F	VP:	150.5 mmhg at 20°C
Sol. (water):	8200 mg/l at 20°C		
Sol. (organics):	soluble in acetone; miscible with alcohol, ether and benzene		

Fate and Transport

Volatilization is chloroform's primary means of transport from surface soils and water. In groundwater and in subsurface soil, chloroform remains stable and leaches readily (EPA, 1984). In the atmosphere, chloroform is hydroxylated to form phosgene and chlorine oxide, with small quantities returning, in precipitation, as chloroform (EPA, 1984).

Pharmacokinetics

Fry, et al. (1972) and Brown, et al. (1974) report that both humans and animals absorb approximately 100 percent of ingested chloroform through the gastrointestinal lining. When inspired, up to 77 percent of chloroform is absorbed by lung tissues (EPA, 1984).

When absorbed by the body, chloroform is distributed to all organs, with high concentrations found in the nervous tissues (IARC, 1979). In rats injected with radio-isotopically labelled chloroform, 75 percent of the radioactivity was expired within 18 hours, all but 5 percent as chloroform (IARC, 1979). The majority of the retained chloroform was metabolized in the kidneys and liver. Most of the chloroform ingested by monkeys was excreted in the urine unchanged (IARC, 1979).

Human Toxicity

Noncarcinogenic Effects

Systemic Effects

Chronic exposure to chloroform in humans results primarily in effects on the central nervous system and, to a lesser degree, the liver, kidneys, and heart (EPA, 1984). One study reported severe digestive disturbances, mental dullness and lassitude in workers exposed to 80 to 240 ppm (ACGIH, 1984). Symptoms appeared to be dose related in the same workers. Another reported enlarged livers in 25 percent of workers handling chloroform at a chemical plant (ACGIH, 1984).

Acute exposure to chloroform is known to be fatal in humans. Death from cardiac arrest and kidney and liver damage as a result of acute exposure (unknown concentration) in chemical plant workers has been noted (IARC, 1979).

In laboratory rats, doses between 90 and 180 mg/kg-bw/day resulted in an increased incidence of noncancerous respiratory disease. Lower doses, 60 mg/gh-bw/day, resulted in lowered body weight, decreased liver weight and decreased levels of serum cholinesterase (EPA, 1984). In another study, researchers reported necroses of the liver and gonad dysfunction at dose levels of 150 and 410 mg/kg-bw/day (EPA, 1985).

Teratogenic and Other Developmental Effects

Chloroform is known to be highly fetotoxic. Decreased body weight and an increase in fetal resorption has been noted in Sprague-Dawley rats (ACGIH, 1984). Another study reported acaudia, decreased crown-rump length, imperforated anus, missing ribs and delayed skeletal ossification in Sprague-Dawley rats that inhaled chloroform for 7 hours/day on days 6-15 of gestation at dose levels between 30 and 300 ppm.

Murray et al. (1979) reported an increased incidence of cleft palate in CF/1 mice exposed to 100 ppm for 7 hours/day on days 6-15 of gestation.

Mutagenic Effects

IRIS reports that the majority of tests for genotoxicity of chloroform have been negative. These negative results include covalent binding to DNA, mutation in *Salmonella*, a *Drosophila* sex-linked recessive test for DNA damage, a micronucleus test, and transformation of BHK cells.

IRIS states, however, that DiRenzo (1982) reported binding to radiolabeled chloroform to calf thymus DNA following metabolism by rat liver microsomes, and Callen et al. (1980) found that chloroform caused mitotic recombination in *Saccharomyces.*

Carcinogenic Effects

Although there have been no epidemiologic studies of chloroform's effects on humans, case studies have consistently reported increased levels of bladder, colon, and rectal cancer in populations exposed to relatively high chloroform levels in the drinking water (IRIS). Other suspected carcinogens were present, however in these water supplies.

Numerous animal studies have been performed that indicate chloroform to be carcinogenic. NCI (1976) reported an increase in malignant mammary tumors in female rats given 60 mg chloroform/kg-bw/day for 96 weeks in a toothpaste base. Male mice, given the same dosage, exhibited an increase in kidney tumors. A significant increase in renal tumors was observed in Osborne-Mendel rats administered chloroform in drinking water at 1800 mg/L for 104 weeks (IRIS).

In a major study performed at the Huntington Research Center, no carcinogenic effects were noted in Beagle dogs, Sprague-Dawley rats, and in 3 of 4 strains of experimental mice (ACGIH, 1984). In the fourth strain, the incidence of renal tumors increased in male ICI-Swiss mice when given 60 mg/kg/day (IARC, 1979).

Ecotoxicity

Chloroform is not known to be strongly bioaccumulated in a food chain.

Further information concerning chloroform's ecological effects was not located in the available literature.

Standards, Criteria and Guidelines

EPA Class B2 Carcinogen

Oral Slope Factor:	6.1×10^{-3} $(mg/kg/day)^{-1}$
Chronic Oral RfD:	1×10^{-2} mg/kg/day
Subchronic Oral RfD:	1×10^{-2} mg/kg/day
MCL:	0.10 mg/L (total trihalomethanes)

BIBLIOGRAPHY

American Conference of Governmental Industrial Hygienists. 1984. *Documentation of the Threshold Limit Values.*

Brown, D.M., P.F. Langley, D. Smith, and D.C. Taylor. 1972. Metabolism of Chloroform, I, The Metabolism of ^{14}C-Chloroform by Different Species, *Xenobioticz*, 4: 151-163. (Cited in EPA, 1984).

Fry, J.T. Taylor and D.F. Hathaway. 1972. Pulmonary Elimination of Chloroform and its Metabolites in Man, *Arch. Int. Pharmacodyn.*, 196: 98-111. (Cited in EPA, 1984).

Heywood, R., et al. 1979. Safety evaluation of toothpaste containing chloroform, III. Long-term study in beagle dogs. *J. Environ. Pathol. Toxicol.*, 2:835-851. (Cited in IRIS).

International Agency for Research on Cancer (IARC). 1979. *Monographs on the Evaluation of The Carcinogenic Risk of Chemicals to Humans.* Vol. 20 p. 410.

Murray, F.J., B.A. Schwetz, J.G. McBride, and R.E. Staples. 1979. Toxicity of Inhaled Chloroform in Pregnant Mice and Their Offspring. *Toxicol. Appl. Pharmacal.* 50: 515-522. (Cited in EPA, 1984).

NCI (National Cancer Institute). 1976. Report on Carcinogenesis Bioassay of Chloroform, NTIS PB-264-018. (Cited in EPA, 1984).

NIOSH. 1987. *Pocket Guide to Chemical Hazards.*

Palmer, A.K., A.E. Street, F.J.C. Roe, A.N. Worden, and N.J. Van Abbe. 1979. Safety Evaluation of Toothpaste Containing Chloroform, II. Long Term Studies in Rats, *J. Environ. Pathol. Toxicol.*, 2: 821-83. (Cited in EPA, 1988).

Sittig, M. 1991. *Handbook of Toxic and Hazardous Chemicals.*

U.S. EPA. *Drinking Water Regulations and Health Advisories.*

U.S. EPA. 1984. *Health Effects Assessment for Chloroform.* EPA 540/1-86/010.

U.S. EPA. *Health Effects Assessment Summary Tables (HEAST).*

U.S. EPA. *Integrated Risk Information System (IRIS).*

U.S. EPA, OERR. *CERCLA Compliance with Other Laws Manual Interim Final.* August, 1988.

U.S. EPA. 1986. *Quality Criteria for Water.* EPA/440/5-86-001.

DICHLOROBENZENE

Use

The compound dichlorobenzene (DCB) has three geometric isomers. 1,2-DCB is a pale yellow liquid with a pleasant, aromatic odor. Its major uses are as a process solvent in the manufacturing of toluene diisocyanate and as an intermediate in the synthesis of dyestuffs, herbicides, and degreasers. Information is not available regarding the use of 1,3-DCB. It may occur as a contaminant of 1,2-DCB and 1,4-DCB. 1,4-DCB is a colorless solid with a mothball-like odor. It is used primarily as an air deodorant and an insecticide, which account for 90 percent of the total production of this isomer (Sittig, 1991).

Physical and Chemical Properties

Chemical Formula: $C_6H_4Cl_2$

	BP: 180.5°C
MW: 147.0 25°C	FP: -17.03°C
Sol. (Water): 154 mg/l at 25°C	VP: 1.5 mm Hg at 20°C

Sol. (organics): Miscible with alcohol, ether, and benzene

Fate and Transport

Dichlorobenzenes exist primarily in a vapor phase in the atmosphere and react with photochemically produced hydroxyl radicals (EPA, 1987). Pankow et al. (1984), detecting dichlorobenzenes in rain water, suggested washout as a possible means of atmospheric removal.

Several studies in the Great Lakes area (Oliver and Nicol, 1982; Oliver, 1983; Oliver and Charlton, 1984) have revealed adsorption to sediments as a major fate process for dichlorobenzenes. Oliver and Nicol (1982) found dichlorobenzenes to be persistently present in Lake Ontario sediment cores. Although Lyman et al. (1982) illustrated the potential of dichlorobenzenes to volatilize from the water column, the U.S. EPA (1987) reports that adsorption to sediments will greatly reduce this fate process.

Swann et al. (1984) reports that, based on the range of log octanol/water partition coefficients (3.38 - 3.60), dichlorobenzenes can be expected to be adsorbed moderately to tightly in soils. The ability of dichlorobenzenes to leach from soils into ground water was illustrated by Page (1981) and Hutchins et al. (1983). The U.S. EPA (1987) reports that volatilization may occur from surface soil but suggests that this is a less important fate process. Haider et al. (1974) reports that, under aerobic conditions, slow biodegradation in soil may take place.

Pharmacokinetics

Ware and West (1977) and U.S. EPA (1985) have concluded that all three dichlorobenzene isomers (1,2-, 1,3-, and 1,4-) are absorbed through the gastrointestinal tract of humans and

experimental animals. Studies on two female CFY rats (Hawkins et al., 1980) have revealed the gastrointestinal absorption of 1,4-DCB to be greater than 90 percent.

Ware and West (1977) and U.S. EPA (1985) also concluded that all three dichlorobenzene isomers are absorbed by the lungs of humans and experimental animals. Hawkins et al. (1980) concluded that 1,4-DCB is substantially absorbed from the lungs based on inhalation studies with CFY rats.

Human Toxicity

Noncarcinogenic Effects

Systemic Effects

In an extensive study by NTP (1985), various groups of F344/N rats and B6C3F1 mice were exposed to 1,2-DCB in corn oil by gavage at various concentrations for various durations. Fifty animals of each sex and species were exposed to 0, 60, or 120 mg/kg/day, 5 days/week for 103 weeks. No significant adverse effects occurred. Ten animals of each sex and species exposed to 0, 30, 60, 125, 250, or 500 mg/kg/day, 5 days/week, for 13 weeks exhibited liver necrosis at the 250 mg/kg/day dose level. Male rats exhibited death, degeneration and necrosis of the liver, lymphocyte depletion in the spleen and thymus, and renal tubular degeneration at the 500 mg/kg/day dose level. Slight decreases in hemoglobin, hematocrit, and red blood cell counts occurred in rats exposed to this high dose.

Rats dosed by gavage with 1,2-DCB at 18.8, 188, or 376 mg/kg/day, 5 days/week for 192 days exhibited increased liver and kidney weights at 188 mg/kg/day and liver pathology and increased spleen weight at 376 mg/kg/day. No effects were observed at the low dose (Hollingsworth et al., 1958). Hollingsworth et al. (1958) also exposed rats, guinea pigs, mice, rats, and monkeys to 1,2-DCB by inhalation at concentrations of 49 or 93 ppm for 7 hours/day, 5 days/week for 6 to 7 months. The only adverse effects reported were reduced body weight gain in rats and reduced spleen weight in guinea pigs at the high dose.

Data regarding the noncarcinogenic systemic effects of 1,3-DCB were not available in the literature reviewed.

In a study by NTP (1986) 50 B6C3F1 mice of each sex and 50 F344 rats of each sex were exposed to 0, 150 (rats only), 300, or 600 (mice only) mg/kg/day of 1,4-DCB 5 days/week for 103 weeks. High-dose male rats exhibited a significantly increased mortality rate relative to controls. High-dose female rats had a 5-7 percent lower mean body weight relative to controls. All the dosed animals except for the male rats exhibited an increased incidence of nonneoplastic nephropathy, characterized by renal tubular atrophy, degeneration

and regeneration; tubular dilation; thickening of the basement membrane; minimal accumulation of interstitial collagen; and the presence of granular casts.

Loeser and Litchfield (1983) exposed groups of 76-79 male and 76-79 female Alderly Park Wistar-derived rats to 0, 75, or 500 ppm of 1,4-DCB, 5 hours/day, 5 days/week for 76 weeks. No immediate effects on body weight, food or water consumption, mortality rate, blood biochemistry, hematology, or the histology of major organs were observed. Thirty-six weeks following treatment, however, those rats exposed to the 500 ppm dose level exhibited increased liver, lung, kidney, and heart weights and a "slightly" elevated urinary coproporphyrin levels.

Teratogenic and Other Developmental Effects

Hayes (1985) exposed pregnant F344/N rats and New Zealand rabbits by inhalation to 0, 100, 200, or 400 ppm of 1,2-DCB, 6 hours daily on days 6 to 15 (rats) or 6 to 18 (rabbits) of gestation. Body weight gain was lower in rats at all doses and in rabbits at 400 ppm during the first 3 days of exposure. Liver weights (absolute and relative) were increased in rats at 400 ppm. No developmental toxicity was observed at any dose.

Data regarding the teratogenicity of 1,3-DCB were not available in the literature reviewed.

Loeser and Litchfield (1983) summarized a report by Hodge et al. (1977) in which groups of 20 pregnant SPF rats were exposed to 0, 75, 200, or 500 ppm of 1,4-DCB for 6 hours/day on days 6-15 of gestation. No evidence of maternal toxicity was observed. One fetus in each group was reported to have a malformation. No significant teratogenic, embryo, or fetotoxic effects were associated with inhalation exposure to 1,4-DCB. Hayes et al. (1985) found no evidence of teratogenicity, embryotoxicity, or fetotoxicity in a similar study with New Zealand rabbits.

Mutagenic Effects

1,2-DCB was not mutagenic in *S. typhimurium* strains TA98, TA100, TA1535, or TA1537 with and without rat or hamster liver homogenates at concentrations as high as 333 µg/plate (NTP, 1985). Lawlor et al. (1979) reported that 1,2-DCB did not produce reverse mutations in TA98, TA100, TA1535, TA1537, or TA1538 with and without rat liver homogenates. Prasad and Promer (1968), however, did report an increase in the frequency of mutations in the auxotrophic strain of *Aspergillus nidulans* following exposure to 1,2-DCB. Similarly, Zapata-Gayan et al. (1982) reported a statistically significant increase in chromosomal alterations in workers occupationally exposed to 1,2-DCB vapors for 4 days (8 hours/day).

Prasad and Promer (1968) report that an increase in the number of revertants of an auxotrophic strain of *Aspergillus nidulans* occurred when spores were treated with 1,3-DCB. However, the increase, however, was not statistically significant.

1,4-DCB was not mutagenic in *S. typhimurium* strains TA98, TA100, TA1535, TA1537, and TA1538 with or without rat liver microsomal activation (Lawlor et al., 1979; NTP, 1986). NTP (1986) found that 1,4-DCB did not increase the mutation frequency in cultivated L5178Y/TI$^{+/-}$ mouse lymphoma cells with or without metabolic activation, nor did it increase the frequency of sister-chromatid exchange or chromosomal aberrations in Chinese Hamster ovaries. Several studies reviewed by Loeser and Litchfield (1983) revealed no signs of mutagenicity as well.

Carcinogenic Effects

The NTP (1985) exposed groups of 50 F344N rats/sex and 50 B6C3F1 mice/sex to 0, 60, or 120 mg/kg/day of 1,2-DCB by gavage in corn oil, 5 days/week for 103 weeks. No statistically significant increases in tumors was observed in the rats. Mice exhibited an increase in the incidence of malignant histiocytic lymphoma. Male mice had an increased incidence of alveolar and bronchiolar carcinomas. One high-dose male had a testicular interstitial cell tumor. Contrary to these findings, male mice exhibited a decrease in the incidence of hepatocellular adenomas and carcinomas.

Data regarding the carcinogenicity of 1,3-DCB were not available in the literature reviewed.

Fifty male and 50 female B6C3F1 mice and 50 female F344/N rats were exposed to 0, 300, or 600 mg/kg/day of 1,4-DCB in corn oil by gavage for 5 days/week for 103 weeks in an NTP (1986) bioassay. Fifty male F344/N rates were exposed to 0, 150, or 300 mg/kg/day for the same duration. Mice exhibited a significant increase in the incidence of hepatocellular adenomas and/or carcinomas. Male rats exhibited a significant increase in the incidence of renal tubular adenocarcinoma and adenoma.

No treatment-related increase in the incidence of tumors was observed in groups of 75-79 Alderly Park Swiss mice or Wistar-derived rats exposed to 0, 75, or 500 ppm 1,4-DCB for 5 hours/day, 5 days/week for 57 and 76 weeks, respectively (Loeser and Litchfield, 1983).

Ecotoxicity

ICF (1985) reports that all the 48- and 96-hour LC_{50} values for *Daphnia* and bluegills tested under static conditions are; 2,440 and 5,590 µg/l (1,2-DCB); 28,100 and 5,020 µg/l (1,3-DCB); and 11,000 and 4,280 µg/l (1,4-DCB), respectively. The 96-hour LC_{50} values around 3,000 µg/l were obtained in two flow through tests using fathead minnows and rainbow trout. The fathead minnow has a chronic toxicity value of

2,000 µg/l. A whole body bioconcentration factor of approximately 80 was reported in the bluegill. In the freshwater alga *Selenastrum capricornutum,* the 96-hour median effect levels for chlorophyll *a* and cell numbers are 179,000 and 149,000 µg/l, respectively.

In saltwater systems, acute values for the mysid shrimp and sheepshead minnow were 1970 and 9,660 µg/l, respectively. No saltwater chronic values are available. The 96-hour median effect levels for chlorophyll *a* and cell numbers in the saltwater alga *Skeletonema capricornutum* are 44,200 and 44,100 µg/l, respectively.

Standards, Criteria, and Guidelines

1,4-DCB EPA Class C Carcinogen

Oral Slope Factor:	1,4-DCB: 2.4×10^{-2} $(mg/kg/day)^{-1}$
Chronic Oral RFD:	1,4-DCB: 3.00×10^{-1} mg/kg/day
Subchronic Oral RfD:	1,4-DCB: 3.00×10^{-1} mg/kg/day
MCL:	1,4-DCB: 75 µg/L
AWQC:	Acute: 1,120 µg/L
	Chronic: 763 µg/L

BIBLIOGRAPHY

Haider, K., et al. 1974. Degradation of Chlorinated Benzenes, Phenols, and Cyclohexane Derivatives by Benzene and Phenol Utilizing Soil Bacteria Under Aerobic Conditions. *Arch. Microbiol.* 96:183-200. (Cited in HEA).

Hawkins, D.R., et al. 1980. The Distribution, Excretion, and Biotransformation of p-dichloro-(^{14}C)benzene in Rats After Repeated Inhalation, Oral, and Subcutaneous Doses. *Xenobiotica.* 10(2):81-95. (Cited in HEA).

Hayes, W.C., et al. 1985. Teratogenic Potential of Inhaled Dichlorobenzenes in Rats and Rabbits. *Fund. Appl. Toxicol.* 5(1):190-202. (Cited in HEA).

Hollingsworth, R.L., et. al. 1958. Toxicity of σ-dichlorobenzene. Studies on animals and industrial experience. *A.M.A. Arch. Indust. Health.* 17:180-187. (Cited in IRIS).

Hutchins, J.R., et al. 1983. Trace Organic Contamination of Ground Water from a Rapid Infiltration Site: A Laboratory-Field Coordinated Study. *Environ. Toxicol. Chem.* 2:195-216. (Cited in HEA).

ICF Clements Associates, Inc. 1985. *Chemical, Physical, and Biological Properties of Compounds Present at Hazardous Waste Sites.*

Lawlor, T., et al. 1979. Evaluation of the Genetic Activity of Nine Chlorinated Phenols, Seven Chlorinated Benzenes, and Three Chlorinated Hexanes. *Environ. Mutagen.* 1:143. (Cited in HEA).

Loeser, E. and M.H. Litchfield. 1983. Review of Recent Toxicology Studies on ℘-Dichlorobenzene. *Food Chem. Toxicol.* 21(6):825-832. (Cited in HEA).

Lyman, W.J., et al. 1982. *Handbook of Chemical Property Estimation Method.* McGraw Hill Book Co., New York. pp. 15-13-15-21. (Cited in HEA).

NTP (National Toxicology Program). 1985. Toxicology and Carcinogenesis studies of 1,2-dichlorobenzene (σ-dichlorobenzene) (CAS No. 95-50-1) in F344/n rats and B6C3F1 mice (gavage studies) NTP TR 255. NIH Publ. No. 86-2511. (Cited in IRIS).

NTP (National Toxicology Program). 1986. Toxicology and Carcinogenesis Studies of 1,4-Dichlorobenzene in F344/N Rats and B6C3F1 Mice. Galley Draft. U.S. DHHS, P.H.S. NIH Tech. Rep. Ser. No. 319. (Cited in HEA).

Oliver, B.G. 1983. Chlorinated Contaminants in the Niagara River and Adjacent Lake Ontario. In: *Symp. Am. Chem. Soc., Div. Environ. Chem. 186th Nat'l. Mtg.* 23:421-422. (Cited in HEA).

Oliver, B.G. and M.N. Charlton. 1984. Chlorinated Organic Contaminants on Settling Particulates in the Niagara River Vicinity of Lake Ontario. *Environ. Sci. Technol.* 18:903-908. (Cited in HEA).

Oliver, B.G. and K.D. Nicol. 1982. Chlorobenzenes in Sediments, Water, and Selected Fish From Lakes Superior, Huron, Erie, and Ontario. *Environ. Sci. Technol.* 16:532-536. (Cited in HEA).

Page, G.W. 1981. Comparison of Ground Water and Surface Water for Patterns and Levels of Contamination by Toxic Substances. *Environ. Sci. Technol.* 15:1475-1481. (Cited in HEA).

Pankow, J.F., et al. 1984. Trace Organic Compounds in Rain. I. Sampler Design and Analysis by Absorption/Thermal Desorption (ATD). *Environ. Sci. Technol.* 18:310-318. (Cited in HEA).

Prasad, I. and D. Pramer. 1968. Mutagenic Activity of Some Chloroanilines and Chlorobenzenes. *Genetics.* 60:212-213 (abstr.) (Cited in IRIS).

Sittig, M. 1991. *Handbook of Toxic and Hazardous Chemicals.*

Swann, R.L., et al. 1984. A Rapid Method for the Estimation of the Environmental Parameters Octanol Water Partition Coefficient Soil Sorption Constant Water to Air Ratio and Water Solubility. *Res. Rev.* 85:17-28. (Cited in HEA).

U.S. EPA. 1991. *Drinking Water Regulations and Health Advisories.*

U.S. EPA. 1985. *Health Assessment Document for Chlorinated Benzenes.*

U.S. EPA. 1987. *Health Effects Assessment for Dichlorobenzenes* (HEA).

U.S. EPA. Integrated Risk Information System (IRIS).

U.S. EPA. *Health Effects Assessment Summary Tables (HEAST).*

U.S. EPA, OERR. *CERCLA Compliance With Other Laws Manual Interim Final.* August, 1988.

U.S. EPA. 1986. *Quality Criteria for Water.* EPA 440/5-86-001. 1986.

Ware, S.A. and W.L. West. 1977. Investigation of Selected Potential Environmental Contaminants: Halogenated Benzenes. U.S. EPA, OTS, Wash., D.C. 20460. Final Report. *EPA 540/2-77-044.* (Cited in HEA).

Windholz, M., Ed. 1983 *The Merck Index 10th ed.,* Merk and Co., Inc. Rahway, N.J..

Zapata-Gayon, C., et al. 1982. Clastogenic Chromosomal Aberrations in 26 Individuals Accidentally Exposed to Ortho-Dichlorobenzene Vapors in the National Medical Center in Mexico City. *Arch. Environ. Health.* 34(4):231-235. 1982. (Cited in IRIS).

1,2 DICHLOROETHANE

Use

1,2 dichloroethane is a thick, man-made liquid that is volatile and possesses a sweet odor. It is used as a precursor in the production of vinyl chloride and numerous industrial degreasers. It can be found in cleaning agents and pesticides and also in such household items as adhesives and paint removers (ATSDR, 1989). 1,2 dichloroethane is also used as a gasoline additive.

Chemical and Physical Properties

Chemical formula: $C_2H_4Cl_2$

MW:	98.97	BP:	83.5°C
SG:	1.253 at 20°C	MP:	-35.4°C
FP:	15°C	VP:	63.8 mmhg at 20°C

Sol.(water): 8690 mg/l at 20°C
Sol.(organics): miscible with alcohol, chloroform and ether

Fate and Transport

The primary avenue of exposure to 1,2 dichloroethane is through the air. The majority of releases of 1,2 dichloroethane occur from accidental spills or improper disposal techniques. When released to surface waters, 1,2 dichloroethane volatilizes to the atmosphere within three days. In the atmosphere, it degrades, through hydroxylation, within two to three months. Because it does not sorb well into soils, 1,2 dichloroethane is readily transported to ground water where it may remain for years (EPA, 1985).

Pharmacokinetics

1,2 dichloroethane is readily absorbed through the tissues of the lungs following inhalation and is respired rapidly (ATSDR, 1989). In a separate study, it was reported that nursing women exposed to 0.063 ppm 1,2 dichloroethane in the workplace rapidly accumulated it in breast milk. Maximum concentrations were reached within one hour after work ended (ATSDR, 1989).

1,2 dichloroethane is known to absorb, via passive diffusion across the mucous membranes of the gastrointestinal tract. Reports indicate that peak concentrations of 1,2 dichloroethane in rats were reached 15 minutes after oral exposure (ATSDR, 1989). Because of it's lipophilic qualities, 1,2 dichloroethane is expected to accumulate in the body's fatty tissues.

1,2 dichloroethane is expelled from the body in the urine after being metabolized to non-volatile organic compounds. It is thought that when this metabolic process is exhausted through acute exposure to 1,2 dichloroethane, the compound recirculates through the body and causes increased toxic effects.

Human Toxicity

Noncarcinogenic Effects

Systemic Effects

Chronic inhalation exposure to humans is known to cause anorexia, nausea, vomiting, fatigue and nervousness (EPA, 1984). Suveev and Babichenko (1969) reported cold sweats, brachycardia, systolic murmurs and enlarged livers in a high percentage of 12 workers chronically exposed to 1,2 dichloroethane. Numerous studies have reported signs of central nervous system dysfunction amongst occupationally exposed workers.

Kozik (1957) reported increases in gastrointestinal disorders, liver and gall bladder diseases and diseases of the muscle, tendons and neuronal ganglia amongst workers exposed to aircraft glue fumes containing 1,2 dichloroethane.

In a chronic oral exposure study performed by NCI (1978), Osborne-Mendel rats were exposed, through gavage doses, to 47 and 95 mg/kg-bw/day for 78 weeks. A high mortality rate was noted for rats in the high exposure group as early as 15 weeks into the study. The early deaths were attributed to unspecified toxic effects rather than carcinogenic effects. Seventy-two percent of female rats exposed to the high dose died as a result of tumors between 60 and 80 weeks.

Teratogenic and Other Developmental Effects

No teratogenic effects were reported in a study performed by Alumot et al. (1976). Rats were fed diets containing 250 or 500 ppm 1,2 dichloroethane. Litter size, mortality rate and weight of young were not effected. 1,2 dichloroethane is known to accumulate in human and animal fetuses (ATSDR, 1989).

Mutagenic Effects

1,2 dichloroethane was shown to be mildly mutagenic in *Salmonella typhimurium* and in *E. coli*. It also increases the amount of sex-linked recessive-lethal alleles in *Drosophila melanogaster* (EPA, 1985).

Carcinogenic Effects

A statistically significant increase in incidences of colon and rectal cancer in men of age 55 years or older was noted by Isacson (1985) as a result of 1,2 dichloroethane in drinking water. These data may be impertinent because of possible exposure to other contaminants (ATSDR, 1989). No other human carcinogenicity data was found in the available literature.

Numerous animal studies, however, indicate 1,2 dichloroethane to be a carcinogen. Doses as low as 47 mg/kg-bw/day produced tumors in rats and mice when administered by gavage (NCI, 1978). In this study, increases in forestomach squamous cell carcinomas and circulating system hemangiosarcomas were noted. Alveolar adenomas, hepatocellular carcinomas and endometrial sarcomas were all noted in mice of both sexes. Mammary adenocarcinomas were observed in female mice and rats (IRIS, 1990).

Inhalation exposure of Wistar and Sprague-Dawley rats and Swiss mice to 1,2 dichloroethane did not result in an increase in tumor incidence, although severe toxic effects were noted in Sprague-Dawley rats exposed to 250 ppm for 7 hours/day, 5 days/week for 78 weeks by Maltoni et al. (1980).

Ecotoxicity

1,2 dichloroethane is known to be less toxic to aquatic animals than most chlorinated ethanes. No information regarding effects to plants or terrestrial animals was found in the available material.

Standards, Criteria and Guidelines

EPA Class B2 Carcinogen

Oral Slope Factor:	9.1×10^{-2} $(mg/kg/day)^{-1}$
Inhalation Slope Factor:	9.1×10^{-2} $(mg/kg/day)^{-1}$
Chronic Oral RfD:	NA
Chronic Inhalation RfD:	NA
Subchronic Oral RfD:	NA
Subchronic Inhalation RfD:	NA
MCL:	5 µg/L
AWQC:	Water and Fish Consumption - 0.94 µg/L
	Fish Consumption - 243.0 µg/L

BIBLIOGRAPHY

Agency for Toxic Substances and Disease Registry (ATSDR), *Toxicological Profile for 1,2 Dichloroethane,* December 1989.

Alumot, E., Nachtomi, E. Mandel, P. Holstein, A. Bondi and M. Hetrzberg, Tolerance and Acceptable Daily Intake of Chlorinated Fumigants in the Rat Diet, 1976, *Food Cosmet. Toxicol.*, 14(2): 105-110, (Cited in EPA, 1985).

American Conference of Governmental Industrial Hygienists (ACGIH), *Documentation of the Threshold Limit Values,* 1984.

Kozik, I., Problems of Occupational Hygiene in the Use of Dichloroethane in the Aviation Industry, 1957, *Gig. Tr. Prof. Zabol.*, 1: 31-38, (Rus), (Cited in EPA, 1984)

Maltoni, C., L. Valgimigli and C. Scarnato, In: Banbury Report No. 5, Ethylene Dichloride: A Potential Health Risk, 1980, B. Ames, P. Infante and R. Reitz, Ed. Cold Spring Harbor Laboratory, P. 3-33, (Cited in EPA, 1984).

NCI (National Cancer Institute) Bioassay of 1,2-Dichloroethane for Possible Carcinogenicity, 1978, NCI Carcinogenesis Technical Report Series No. 55, DHEW Publ, No. (NIH) 78-1376, Government Printing Office, Washington, D.C., (Cited in EPA, 1984).

Sittig, Marshal, *Handbook of Toxic and Hazardous Chemicals*, 1991.

Spencer et al., 1951 (full reference not given in IRIS).

Suveev, I.M. and M.E. Babichenko, Clinical Picture and Treatment of Acute Poisoning with Dichloroethane Vapors, 1969, *Gig. Tr. Prof. Zabol.*, 13(1): 50-51, (Rus), (Cited in EPA, 1984).

U.S. EPA, *Drinking Water Regulations and Health Advisories.*

U.S. EPA, *Health Effects Assessment for 1,2 Dichloroethane, EPA 540/1-86/002*, 1984.

U.S. EPA, *Integrated Risk Information System (IRIS).*

U.S. EPA, OERR. *CERCLA Compliance With Other Laws Manual Interim Final.* August, 1988.

Van Duren et al., 1979 (full reference not given in IRIS).

1,1-DICHLOROETHYLENE

Use

1,1-Dichloroethylene (1,1-DCE) is a clear liquid with the sweet smell typical of a chlorinated solvent. 1,1-DCE is used in the manufacture of paint, varnish, lacquer, soap and finish removers. It is also frequently used as a solvent for cellulose esters, napthalenes, oils, fats, tar and gum and as a cleaning agent in the dry cleaning industry (Sittig, 1991).

Chemical and Physical Properties

Chemical Formula: CH_2CCl_2

MW: 96.94
SG: 1.218 at 20°C
FP: none
BP: 37°C
MP: -122.1°C
VP: 500 mmHg at 20°C
Sol. (water): 400 mg/l at 20°C
Sol. (organics): slightly soluble in alcohol, ether, acetone, benzene, and chloroform.

Fate and Transport

Volatilization is the primary route of removal of 1,1-DCE from surface waters. Once in the atmosphere 1,1-DCE is photo-oxidized through hyroxylation. 1,1-DCE will most likely volatilize from surface soils with low organic content but will adsorb to any organic matter present (ICF, 1985). It is speculated, because of work done with similar compounds, that 1,1-DCE would leach readily from soils and would migrate with ground water (EPA 1985).

Pharmacokinetics

1,1-DCE is known to be absorbed rapidly into the digestive tract of rats upon oral administrations (EPA 1985). McKenna et al. (1978) reported the rapid appearance of labelled 1,1-DCE in the urine and expired air of rats given an intragastric dose of ^{14}C-labeled 1,1-DCE.

Andersen et. al., (1979) exposed fasted male rats to various concentrations of 1,1-DCE in a closed chamber. They observed an initial rapid phase followed by a slow phase of uptake. They concluded that the rapid phase represented whole body equilibrium while the slow phase represents metabolism.

Human Toxicity

Noncarcinogenic Effects

Systemic Effects

In 3 studies (Rampy et al., 1977; Quast et al., 1983) of lab animals orally exposed to 1,1-DCE, no significant effects were noted other than an increased incidence of cytoplasmic vacuolization of hepatocytes.

Inhalation studies revealed that subchronic exposure can lead to liver and kidney damage. Prendergast et al. (1967) exposed rats, guinea pigs, rabbits, dogs and monkeys to atmospheric concentrations of 1,1-DCE ranging from 20 to 395 mg/m^3 for up to 90 days. Continuous exposure to 189 mg/m^3 produced dose related mortality in guinea pigs and monkeys. At high doses, growth depression was noted in all species, as were renal lesions, hepatic lesions and/or enzyme alterations.

The U.S. EPA (1985) reports that chronic studies, both inhalation and oral, generally resulted in hepatocellular fatty changes and periportal hepatocellular hypertrophy. This condition is reversible upon termination of treatment. No increase in mortality, other than from carcinogenesis, was noted in any of the studies.

Teratogenic and Other Developmental Effects

Short et al. (1977) and Murray et al. (1979) both noted signs of fetal toxicity, skeletal alterations and soft-tissue alterations in rats, rabbits and mice as a result of inhalation. The alterations were considered to be manifestations of maternal toxicity.

Mutagenic Effects

Drevon and Kuroki (1979) reported that 1,1-DCE was not mutagenic for V79 cells exposed to vapor in vitro and Cerna and Kypenova (1977) found that it did not produce chomosomal aberrations in bone marrow cells of ICR mice given single or repeated i.p. treatment in vivo.

Reitz et. al., (1980) reported CD-1 mice and Sprague-Dawley rats exposed in vivo to 1,1-DCE showed signs of DNA alkylation and subsequent repair which was specific to liver and kidney, with the kidney of both species exhibiting higher alkylation.

Carcinogenic Effects

Ott et al. (1976) investigated occupational exposure of 138 Dow Chemical Company workers to 1,1-DCE. No statistically significant differences were noted between workers exposed to various concentration of 1,1-DCE.

Of eighteen studies performed on laboratory animals, only one was deemed acceptable in implying 1,1-DCE as a carcinogen (IRIS). Maltoni et al. (1985) exposed Swiss mice to 10 and 25 ppm 1,1-DCE for 4-5 days/week for 12 months. A statistically significant increase in kidney adenocarcinoma was noted in the male Swiss mice. An increase in the incidence of mammary carcinomas was noted, but no dose-response characteristics were observed (IRIS). In a similar study Maltoni noted mammary tumors in Sprague-Dawley rats exposed to concentrations of 10 and 100 ppm 1,1-DCE (IRIS).

Ecotoxicity

1,1-DCE is not extremely toxic to freshwater or saltwater organisms, with LC_{50} values ranging between 80 and 200 mg/l (ICF, 1985).

No data regarding the toxicity of 1,1-DCE to aquatic or terrestrial organisms were located in the literature reviewed.

Standards, Criteria and Guidelines

EPA Class C Carcinogen

Oral Slope Factor:	6.0×10^{-1} $(mg/kg/day)^{-1}$
Chronic Oral RfD:	9.0×10^{-3} mg/kg/day
Subchronic Oral RfD:	9.0×10^{-3} mg/kg/day
MCL:	7 µg/L

BIBLIOGRAPHY

Andersen, M.E., et al., The use of inhalation techniques to assess the kinetic constants of 1,1-dichloroethylene metabolism. *Toxicol. Appl. Pharmacol.* 47(2): 395-409. 17979 (cited HEA, 1985).

ICF Clement; *Chemical, Physical and Biological Properties of Compounds at Hazardous Waste Sites,* 1985.

Maltoni, et. al., 1985. (full reference not given in IRIS).

McKenna, M.J. et. al., Metabolism and pharmacokinetics profile of vinylidene chloride in rats following oral administration. *Toxicol. Appl. Pharmacol.* 45(3): 821-835. 1978 (cited in HEA, 1985).

Murray, F. et. al., Emphyotoxicity and fetotoxicity of inhaled or ingested vinylidene chloride in rats and rabbits. *Toxicol. Appl. Pharmacol.* 48: 189-202. 1979 (cited in IRIS).

Ott, M.G., et. a., A health study of employees exposed to vinylidene chloride. *J. Occup. Med.* 18(11): 735-738. 1976 (cited in HEA, 1985).

Prendergast et. al., Effects on experimental animals of long-term inhalation of trichloroethylene, carbon tetrachloride, 1,1,1-trichloroethane, dichlorodifluoromethane, and 1,10dichloroethylene. *Toxicol. Appl. Pharmacol.* 10(2): 270-289. 1967 (cited in HEA, 1985).

Quast, J.F. et. al., A chronic toxicity and oncogenicity study in rats and subchronic toxicity study in dogs on ingested vinylidene chloride. *Fund. Appl. Toxicol.* 3:55-62. 1983 (cited in IRIS).

Rampy, L.W. et. al., Interim results of two-year toxicological studies in rats of vinylidene chloride/incorporated in the drinking water or administered by repeated inhalation. *Environ. Health Perspec.* 21:31-43. 1977 (cited in HEA, 1985).

Short, R.D. et. al., *Toxicity Studies of Selected Chemicals. Task II. The Development Toxicity of Vinylidene Chloride Inhaled by Rats and Mice During Gestation.* Prepared by Midwest Research Inst., Kansas City, MO under Contract 68-01-3242. U.S. EPA, Office of Toxic Substances, Washington, DC EPA 560/6-77-022. 1977 (cited in IRIS).

Sittig, Marshall; *Handbook of Toxic and Hazardous Chemicals,* 1991.

U.S. EPA, *Drinking Water Regulations and Health Advisories.*

U.S. EPA(a); *Health Effects Assessment for 1,1 Dichloroethylene,* 1985.

U.S. EPA; *Integrated Risk Information System (IRIS).*

U.S. EPA, OERR. *CERCLA Compliance With Other Laws Manual Interim Final.* August, 1988.

Van Duren et al., 1979 (full reference not given in IRIS).

1,2-DICHLOROETHYLENE

Use

1,2-dichloroethylene exists in two isomers, cis 60 percent and trans 40 percent. The toxicity of these two forms varies. At room temperature, 1,2-dichloroethylene is a liquid with a slight acrid, ethereal odor. It is also known as acetylene dichloride and symdichloroethylene.

It is used as a solvent for acetylcellulose, resins, and waxes. 1,2-dichloroethylene is utilized in the extraction of rubber, in the extraction of oils and fats from fish and meat, as a refrigerant, and in the manufacture of pharmaceuticals and artificial pearls (Sittig, 1991).

Chemical and Physical Properties

Chemical Formula: ClCH - CHCl
MW: 96.94
SG: 1.2565 at 20°C
Sol. (water): 600 mg/liter
Sol. (organics): Miscible with alcohol, ether, and acetone. Very soluble in benzene and chloroform.

BP: 47.5°C
MP: -50°C
VP: 200 mmHg at 14°C
FP: 3°C (undef. isomers)

Fate and Transport

The half-life of the trans isomer of this compound has been estimated by the EPA to be 1-6 days with the cis isomer being even lower (U.S. EPA, 1984). Volatilization is probably the main means of dispersion (ICF, 1985).

1,2-dichloroethylene is broken down rapidly by hydroxylation. Some may be absorbed by water vapor and returned to the earth in precipitation, however. (ICF, 1985).

Given that both isomers have low octanol/water partition coefficients, it is expected that evaporation will be the major fate of this compound in surface soils (U.S. EPA, 1984). Tabak et al. (1981) concluded that biodegradation of 1,2-dichloroethylene in subsurface soil is likely to be a slow process. Therefore, the compound is expected to leach from subsurface soil into ground water. In fact, Page (1981) reported a frequency of 51 percent for 1,2-t-dichloroethylene in New Jersey ground waters.

Pharmacokinetics

The U.S. EPA (1980) has estimated that "virtually 100 percent of ingested DCE (dichloroethylene) may be absorbed systematically" based on the studies of Daniel (1963) and Monster et al. (1976) using trichloroethylene. These same studies led the U.S. EPA (1980) to estimate that "35 to 50 percent of inhaled DCE... may be absorbed systematically."

Human Toxicity

Noncarcinogenic Effects

Systemic Effects

Springer (1965) administered a mixture of the 1,2- dichloroethylene isomers to rats for seven weeks at concentrations of 0.05, 0.25, 0.5 or 1.0 g/kg. Whether these were daily, weekly or total doses is unclear. No adverse effects were reported at any dose level. Barnes et al. (1985) reported no dichloroethylene-induced changes in gross pathology or terminal body weight at any dose level when male and female CD-1 mice were exposed to the trans isomer in their drinking water at concentrations of 0.1, 1.0 or 2.0 mg/ml.

Contrary to these reports, Jenkins et al. (1974) reported increases in a series of hepatic enzymes in rats, indications of hepatotoxicity resulting from single dose exposures of 400 or 1500 mg/kg of cis-1,2-dichloroethylene introduced by gavage in corn oil. The authors suggested that the cis isomer appears to be slightly more hepatotoxic than the trans isomer with respect to these endpoints. Freundt et al. (1977) found progressive damage to the lungs and fatty changes in the liver when groups of six female Wistar rats were exposed to 100 ppm atmospheric concentrations of trans-1,2-dichloroethylene 8 hrs/day, 5 days/week for 1,2,8 or 16 weeks.

Freundt and Machotz (1978) found that exposure of rats to 100 ppm of cis-1,2-dichloroethylene for 8 hours resulted in inhibition of the MFO system as measured by hexobarbital sleeping time, zoxazolamine paralysis and formation of amino-antipyrine from aminopyrine. They also reported that the cis isomer was a more potent inhibitor than the trans isomer.

Teratogenic and Other Developmental Effects

Pertinent data regarding the teratogenicity of either isomer of 1,2-dichloroethylene were not found in the literature reviewed.

Mutagenic Effects

Greim et al. (1975) reported negative results for mutagenicity by either isomer of 1,2-dichloroethylene using *E,coli K12* as the indicator organism. Cerna and Kypernala (1977) found that both isomers were not mutagenic in *Salmonella* tester strains. They did find that the cis isomer produced a dose-dependent increase in mutations using the host-media bioassay and that it induced chromosomal aberrations as indicated by cytogenic analysis of bone marrow cells isolated from given repeated intrapetitoned injections while the trans isomer did not.

Carcinogenic Effects

Pertinent data regarding the carcinogenicity of either isomer of 1,2-dichloroethylene was not found in the literature reviewed. The trans isomer has been evaluated by the U.S. EPA for evidence of human carcinogenic potential, and the cis isomer is classified Class D, not classifiable as to human carcinogenicity.

Ecotoxicity

The U.S. EPA (1986) reports that acute toxicity to freshwater aquatic life occurs at concentrations as low as 11,600 µg/liter and it is expected that it would occur at lower concentrations in species more sensitive than those tested.

They also report that the available data indicate that acute and chronic toxicity to saltwater aquatic life occurs at concentrations as low as 224,000 µg/liter and it is expected that it would occur at lower concentrations in species more sensitive than those tested. (U.S. EPA, 1986).

Standards, Criteria and Guidelines

EPA Class D Carcinogen (cis isomer); no classification for mixed isomers.

Oral Slope Factor:	cis: NA
	trans: NA
	mixed isomers: NA
Chronic Oral RFD:	cis: 1.0×10^{-2} mg/kg/day
	trans: 2.0×10^{-2} mg/kg/day
	mixed isomers: 9.0×10^{-3} mg/kg/day
Subchronic Oral RfD:	cis: 1.0×10^{-1} mg/kg/day
	trans: 2.0×10^{-1} mg/kg/day
	mixed isomers: 9.0×10^{-3} mg/kg/day
MCL:	cis: 70 µg/L
	trans: 100 µg/L

BIBLIOGRAPHY

Barnes, D.W. et al., Toxicology of Trans-1,2-Dichloroethylene in the Mouse. *Drug. Chem. Toxicol.* 8: 373-392 1985 (cited in Iris, 1991).

Cerna, M. and H. Kypernova, Mutagenic Activity of Chlorethylenes Analyzed by Screening System Tests. *Mutat. Res.* 46: 214 1977 (cited in HEA, 1984, a,b).

Daniel, J.W., The Metabolism of ^{36} Ci-labeled Trichloroethylene and Tetrachloroethylene in the Rat. *Biochem. Pharmacol.* 31: 2095-2102 1963 (cited in HEA, 1984, a,b).

Freundt, K.J. et al., Toxicity Studies in trans-1,2-dichloroethylene. *Toxicology* 7: 141-153 1977 (cited in HEA 1984 a,b).

Freundt, K. J. and J. Macholz, Inhibition of Mixed function Oxidase in Rat Liver by trans-and cis 1,2-dichloroethylene. *Toxicology* 10: 131-129 1978 (cited in HEA, 1984 a).

Greim, H. et al., Mutagenicity in Vitro and Potential Carcinogenicity of Chlorinated ethylenes as a function of metabolic oxirane Formation. *Biochem Pharmacol.* 24: 2013 1975 (cited in HEA, 1984 a,b).

ICF Clement Associates, *Chemical, Physical, and Biological Properties of Compounds Present at Hazardous Waste Sites.* September, 1985.

McCauley, P.T. et al. The effect of subacute and subchronic oral exposure to cis-1,2-dichloroethylene in rats. Health Effects Research Laboratory, U.S. EPA, Cincinnati, OH, (Cited in HEAST).

Monster, A.C. et al., Pharmacokinetics of Trichloroethylene in Volunteers influence, of work load and exposure Coxentation. *Ind. Arch. Occup. Environ. Health* 38: 87-102 1976 (cited in HEA, 1984, a,b).

Page, G. W., Comparison of Groundwater and Surface Waters for Patterns and Levels of Contamination by Toxic Substances. *Environ. Sci. Technol.* 15: 1475-1481 1984 (cited in HEA, 1984 a, b).

Sittig, Marshall, *Handbook of Toxic and Hazardous Chemical,* 1991.

Springer, E., No title provided. *Z. Gesomte Hyg. Ihre Grenzgelo* 11: 442 1965 (cited in HEA, 1984 a,b).

Jenkins, L.J. et al., Biochemical effects of 1,1-dichloroethylene in Rats, comparisons with Carbon Tetrachloride and 1,2-dichloroethylene. *Toxicol. Appl. Pharmacol.* 23: 501 1972 (cited in HEA, 1984a).

Tabak, H.H. et al., Biodegradability Studies with Organic Priority Pollutant Compounds. J. *Water Pollut. Control Fed.* 53: 1503-1518 1981 (cited in HEA, 1984a,b).

U.S. EPA, *Drinking Water Regulations and Health Advisories.*

U.S. EPA, *Guidelines and Methodology Used in the Preparation of Health Effects Assessment Chapters of the Consent Decree Water Quality Criteria.* Federal Register 45: 79347: 79357 1980 (cited in HEA, 1984a,b).

U.S. EPA, *Health Effects Assessment for cis-1,2-dichloroethylene.* EPA 540/1-86/015 September, 1984a.

U.S. EPA, *Health Effects Assessment for 1,2-t-dichloroethylene.* EPA 540/1-86/041 September, 1984b.

U.S. EPA, *Health Effects Assessment Summary Tables (HEAST).*

U.S. EPA, *Integrated Risk Information System (IRIS).*

U.S. EPA, OERR. *CERCLA Compliance With Other Laws Manual Interim Final.* August, 1988.

U.S. EPA, *Quality Criteria for Water.* EPA 440/5-86-001. May 1986.

METHYLENE CHLORIDE

Use

Methylene chloride is a widely used industrial degreaser and paint remover. It is also used as a low temperature extractant and as a solvent for oil, fats, waxes and cellulose acetate (Sittig, 1991). Commercially, methylene chloride is used in aerosols as a flammability depressant, as a weight additive and as a caffeine extractant for coffee and tea (BNA, Inc., 1985).

Chemical and Physical Properties

Chemical Formula: $CH_2 Cl_2$

MW: 84.93	BP: 40°C
SG: 1.32 at 20°C	MP: -95.1°C
Sol. (water): 13,200 mg/l at 20°C	JP: 362.4 mmHg at 20°C
Sol. (organics): alcohol and ether.	

Fate and Transport

Methylene chloride is removed from surface soils and water primarily through volatilization. In the atmosphere, methylene chloride is photo-oxidized and broken down by hydroxyl radicals. Its byproducts include carbon dioxide and, to a lesser extent, carbon monoxide and phosgene (ICF, 1985). Atmospheric methylene chloride may be returned to earth via wet and dry deposition (ICF, 1985). It appears as though methylene chloride does not sorb well to soils and is not heavily bioaccumulated. Because of this, methylene chloride likely leaches readily to the groundwater (ICF, 1985).

Pharmacokinetics

Most cases of human absorption of methylene chloride involve inhalation. Methylene chloride reaches a steady state in the body after less than seven hours of continuous exposure. DiVincenzo and Kaplan (1981) exposed groups of volunteers to between 50 and 200 ppm methylene chloride for 7.5 hours. The pulmonary system was the primary route of absorption. Respiration eliminated less than 5 percent of the methylene chloride absorbed. Methylene chloride is metabolized to carbon monoxide in the body.

In the body, methylene chloride is concentrated in adipose tissue. Savolainen et al. (1977) noted that rats exposed to 200 ppm methylene chloride, for 6 hours/day for 5 days concentrated methylene chloride in the brain, blood, liver, and perirenal fat.

Human Toxicity

Noncarcinogenic Effects

Systemic Effects

The National Coffee Association (1982) exposed groups of 85 rats/sex to doses of 5, 50, 125, and 250 mg/kg/day methylene chloride for 2 years. Doses of 50 mg/kg/day and larger resulted in histological alterations of the liver.

Subchronic exposure of rats to methylene chloride caused toxic effects in groups exposed to >100 ppm. Narcosis and lethargy were the two most pronounced effects (EPA, 1974). Chronic inhalation studies on workers occupationally exposed to methylene chloride revealed no indications of increased mortality rates from circulatory heart disease or cancer (EPA, 1989).

Direct contact with methylene chloride causes irritation of the mucous membranes in humans. Lassitude, anorexia, numbness and light-headedness are a few of the side effects of chronic exposure (ICF, 1985). Acute exposure is known to cause heart arrythmia and death in humans and liver and kidney damage in laboratory animals.

Haun et al. (1972) observed no effects in rats exposed via inhalation to 87 mg/m^3.

Teratogenic and Other Developmental Effects

Methylene chloride appears not to cause developmental or teratogenic effects in laboratory animals. Elevated levels of carboxyl hemoglobin, resulting from presence of carbon monoxide as a metabolite, were noted in rat fetuses. Mouse fetuses appear to exhibit advanced ossification of the sternebrae (EPA, 1989).

Mutagenic Effects

Methylene chloride was found to be mutagenic to *Salmonella typhimurium* and was noted to cause mitotic recombination in yeast cells (IRIS).

Carcinogenic Effects

NTP (1986) exposed rats and mice to levels of methylene chloride between 0 and 4000 ppm. A significant increase in mammary adenomas, fibroadenomas, hepatocellular adenomas, and carcinomas was evident. In a separate study, methylene chloride was shown to cause a slight increase in the incidence of hepatocellular carcinomas and neoplastic nodules in female rats. In this study, the National Coffee Association (1983) exposed rats to between 5 and 250 mg methylene chloride/kg/day.

Human case studies concerning occupational exposure to methylene chloride have shown little positive carcinogenic data. Friedlander et al (1978) provided evidence which suggested that methylene chloride increased the incidence of pancreatic tumors (IRIS). This evidence was eventually deemed inconclusive.

Ecotoxicity

Very little pertinent information concerning the toxic effects of methylene chloride on wildlife was located. Acute toxicity levels for saltwater species range between 193,000 and 224,000 mg/l. Saltwater species appear to be more tolerant, with acute toxicity levels ranging between 256,000 and 331,000 mg/l.

Standards, Criteria and Guidelines

EPA Class B2 Carcinogen

Oral Slope Factor:	7.5×10^{-3} (mg/kg/day)$^{-1}$
Chronic Oral RfD:	6×10^{-2} mg/kg/day
Subchronic Oral RfD:	6×10^{-2} mg/kg/day
MCL:	5 µg/L

BIBLIOGRAPHY

Bureau of National Affairs, *Chemical Regulation Reporter,* September 1985.

Bureck, J.D. et al. Physiologically based pharmacokinetics and the risk assessment process for methylene chloride. *Toxicol. Appl. Pharmacol* 87:185-205, 1987, (Cited in IRIS).

DiVincenzo, G.D., F.J. Yanno and B.D. Astill, Human and Canine Exposures to Methylene Chloride Vapor, *Am. Ind. Hyg. Assoc. J.*, 33: 125-135, 1972, (Cited in U.S. EPA, 1989).

Friedlander, B.R., F.T. Hearne and S. Hall, Epidemiologic Study of Employees Chronically Exposed to methylene chloride, 1978, *J. Occup. Med.*, 20:657-666, (Cited in IRIS).

Haun, C.C., E.H. Vernot, K.I. Darmer, Jr., and S.S. Diamond, Continuous Animal Exposure to Low Levels of Dichloromethane AMRL-TR-130, Paper No. R, 1972, In: *Proceedings of the 3rd Annual Conference on Environmental Toxicology*, Wright-Patterson Air Force Base, Ohio, Aerospace Medical Research Laboratory, page 199-208, (Cited in IRIS).

ICF, Clement Associates, *Chemical, Physical and Biological Properties of Compounds Present at Hazardous Waste Sites,* 1985.

National Coffee Association (NCA). *24-month chronic toxicity and oncogenicity study of methylene chloride in rats.* Final Report prepared by Hazleton Laboratories America, Inc. Vienna, VA. (unpublished) 1982 (cited in IRIS).

National Coffee Association (NCA). *Twenty-four month oncogenicity study for methylene chloride in mice.* Final Report prepared by Hazleton Laboratories, America, Inc. Vienna, VA. 1983 (cited in IRIS).

National Toxicity Program (NTP); Toxicology and Carcinogenesis Studies of Dichloromethane (Methylene Chloride) in F344/N Rats and B6C3F1 Mice (Inhalation Studies, 1986; NTP-TRS-306, (Cited in IRIS).

Savolainen, H., P. Ptaffli, M. Tengen and H. Vainio, Biochemical and Behavioral Effects of Inhalation Exposure to Tetrachloroethylene and Dichloromethane, *K. Neuropath, Exptl. Neural.*, 36(6): 941-949, 1977, (Cited in U.S. EPA, 1989).

Sittig, Marshall, *Handbook of Toxic and Hazardous Chemicals*, 1991.

U.S. EPA, *Drinking Water Regulations and Health Advisories.*

U.S. EPA, *Health Effects Assessment for Methylene Chloride,* EPA, 600/1-89/092, 1989.

U.S. EPA, *Health Effects Assessment Summary Tables (HEAST).* FY1991.

U.S. EPA, *Integrated Risk Information System (IRIS).*

U.S. EPA, OERR. *CERCLA Compliance With Other Laws Manual Interim Final.* August, 1988.

TETRACHLOROETHYLENE

Use

Tetrachloroethylene, often called perchloroethylene (PCE), is a clear liquid with an odor similar to that of ether. Its major uses are as a dry-cleaning solvent and as a degreaser. PCE is also used as a fumigant, a chemical intermediate, and medically as an anthelmintic (ACGIH, 1984).

Chemical and Physical Properties

Chemical Formula: C_2Cl_4

MW:	165.83	BP:	121°C
SG:	1.63 at 20°C	MP:	-22.7°C
FP:	none	VP:	14 mmhg at 20°C

Sol. (water): 150 to 200 mg/l at 20°C
Sol. (organics): alcohol, ether and benzene.

Fate and Transport

Tetrachloroethylene volatilizes rapidly when released to surface waters and soils. In the atmosphere, tetrachloroethylene interacts with hydroxyl radicals to produce carbon dioxide, carbon monoxide, and hydrogen chloride (ICF,1985).

In soils, tetrachloroethylene adsorbs to the organic material present. In soils of low organic content, tetrachloroethylene leaches and is transported readily in the ground water (EPA 1985). Tetrachloroethylene is known to degrade slowly in ground water, where it can remain for months to years. Its degradation products in aquatic media are reported to be vinyl chloride and dichloroethylene (EPA, 1985).

Pharmacokinetics

When absorbed into the bloodstream, tetrachloroethylene is distributed mainly to fatty tissues. Much lower concentrations can be found in the blood and liver of humans. Rats absorb tetrachloroethylene into most body tissues, with concentration levels in the brain, lungs, and fat increasing proportionally with exposure. Blood and liver concentrations tend to level off after a three hour period (EPA, 1985).

Only 4 percent of tetrachloroethylene absorbed by humans is metabolized. Metabolites include trichloroethanol, trichloroacetic acid and other unidentified chlorinated products (EPA, 1985). Absorbed tetrachloroethylene is primarily respired through the lungs. Its metabolites are eliminated via the urine, with a half-life of 144 hours (EPA, 1985).

When taken orally, tetrachloroethylene is absorbed through the gastrointestinal lining. Fats and oils are known to facilitate absorption in dogs (EPA, 1984).

Human Toxicity

Noncarcinogenic Effects

Systemic Effects

No significant case studies on human exposure to tetrachloroethylene were located in the available literature, although chronic exposure is reported to effect the central nervous system, mucous membranes, eyes, and skin. Unconsciousness, dizziness and vertigo are reported to have occurred after acute occupational exposure and several fatalities have been reported as a result of massive accidental exposure (unspecified concentrations) (ACGIH, 1984). For mice, the oral LD_{50} has been reported to be 8.85 mg/kg-bw, with the LC_{50} in air reported as 6000 ppm over a 4 hour period (ACGIH, 1984).

Buben and O'Flaherty (1985) reported that Swiss-Cox mice exposed, by gavage to between 20 and 2000 mg tetrachloroethylene/kg-bw exhibited signs of toxicity in the liver. At higher doses, decreased DNA content, increased SGPT and hepatocellular necroses were noted.

Rowe et al. (1952) reported that rats, when exposed to 1600 ppm tetrachloroethylene for 7 hours/day, 5 days/week over a 25 day period, initially exhibited drowsiness and depression. Enlarged livers and kidneys were noted after 4 weeks.

In the same study, Rowe exposed rabbits, guinea pigs and monkeys to 100-400 ppm tetrachloroethylene for 7 hours/day, 5 days/week for approximately 6 months. No abnormal growth, organ function or histopathological findings were noted.

In a study of chronic oral exposure, the National Cancer Institute (NCI) administered, by gavage, doses between 300 and 949 mg/kg/day tetrachloroethylene to Osborne-Mendel rats and B6C3F1 mice. Toxic nephropathy was observed at all dose levels.

Teratogenic and Other Developmental Effects

Tetrachloroethylene is known to cause increased fetal resorption, subcutaneous edema, split sternebrae, and delayed skull ossification in mice and rats after exposure to 300 ppm for 7 hours/day on days 6-15 of gestation (Schwetz et al., 1975).

No information concerning developmental effects on humans was found in the available literature.

Mutagenic Effects

In an abstract, Cerna and Kypenova (1977) reported that tetrachloroethylene caused mutagenic effects in a *Salmonella* strain, but since details of methodology were not presented, the reliability of the experiment has been questioned.

Carcinogenic Effects

Tetrachloroethylene was found to be carcinogenic in mice and rats. No studies with definitive findings are available showing the carcinogenic effects of tetrachloroethylene on humans, although Blair et al. (1979) observed an excess of lung, cervical and skin cancers and a slight excess of leukemia amongst 330 deceased laundry and dry-cleaning workers. The workers, however, were also exposed to carbon tetrachloride and trichloroethylene.

NCI (1977) noted a significant increase in hepatocellular carcinoma in B6C3F1 mice exposed, by gavage, to between 386 and 1072 mg/kg-bw/day, 5 days/week for 78 weeks. No increase in tumor incidence was noted in rats exposed to similar concentrations.

No significant increase in malignant tumors was noted in an inhalation study performed by Rampy et al. (1977) on Sprague-Dawley rats.

Ecotoxicity

Tetrachloroethylene is considered to be moderately toxic to aquatic organisms. Trout were reported to exhibit on LC value of 4,800 µg/l. This was the most sensitive species tested (ICF, 1985)

No information concerning tetrachloroethylene's toxicity to terrestrial organisms was located in the available literature.

Standards, Criteria and Guidelines

EPA Class B2-C Carcinogen

Oral Slope Factor:	5.2×10^{-2} $(mg/kg/day)^{-1}$
Chronic Oral RfD:	1.0×10^{-2} mg/kg/day
Subchronic Oral RfD:	1.0×10^{-1} mg/kg/day
MCL:	0.005 mg/L

BIBLIOGRAPHY

American Conference of Governmental Industrial Hygienists. 1984. *Documentation of the Threshold Limit Values.*

Blair, A., P. Decoufle and D. Grauman. 1979. Causes of Death Among Laundry and Dry Cleaning Workers, *Am. J. Publ. Health*, 69: 508-511. (Cited in EPA, 1988).

Buben, J.A. and E.J. O'Flaherty. 1985. Delineation of the Role of Metabolism in the Hepatotoxicity, of Trichloroethylene and Perchlorothylene: A Dose-Effect Study. 78: 105-122.

Cenna, N. and H. Kypenova. 1977. Mutagenic Activity of Chloroethylenes Analyzed by Screening System Tests, *Mut. Res.* 46 (3): 214-25. (Cited in EPA, 1985).

ICF, Clement. 1985. *Chemical, Physical and Biological Properties of Compounds Present at Hazardous Waste Sites.*

NCI (National Cancer Institute). 1977. Bioassay of Tetrachloroethylene for Possible Carcinogenicity, *NCI Carcinogenesis Tech. Rep. Ser. Co.*, NCI-CGTR-13. (Cited in EPA, 1985).

NTP (National Toxicology Program). 1986. Carcinogenesis bioassay of tetrachloroethylene (perchloroethylene) (CAS No. 127-18-4) in F344 rats and B6C3F1 mice (inhalation study). *NTP Tech. Report Ser. No. 311.* (Cited in HEAST).

Rampay, L.W., J.F. Quast, B.K.J. Leong and P.J. Gehring. 1977. Results of Long Term Inhalation Toxicity Studies on Rats of 1,1,1-Trichloroethane and Perchloroethylene Formulations, In: *International Congress on Toxicology*, Toronto, Canada, page 27. (Cited in EPA, 1985).

Rowe, U.K., D.D. McCollister, H.C. Spencer, E.M. Adams and D.D. Irish. 1952. Vapor Toxicity of Tetrachloroethylene for Laboratory Animals and Human Subjects, *AMA Arch. Ind. Hyg. Occup. Med.*, 5:566-579. (Cited in EPA, 1985).

Schwetz, B.A., B.K.J. Leong, and P.J. Gehring. 1975. The Effect of Maternally Inhaled Trichloroethylene, Perchloroethlyene, Methyl Chloroform, and Methylene Chloride on Embryonal and Fetal Development in Mice and Rats, *Toxicol. Appl. Pharmacal.*, 32: 84-96. (Cited in EPA, 1985).

Sittig, M. 1991. *Handbook of Toxic and Hazardous Chemicals.*

U.S. EPA. *Drinking Water Regulations and Health Advisories.*

U.S. EPA. 1985. *Health Advisory for Tetrachloroethylene,* Office of Drinking Water.

U.S. EPA. 1984. *Health Effects Assessment for Tetrachloroethylene,* EPA 540/1-86/009.

U.S. EPA. *Health Effects Assessment Summary Tables (HEAST).*

U.S. EPA. *Integrated Risk Information System (IRIS).*

U.S. EPA, OERR. *CERCLA Compliance With Other Laws Manual Interim Final.* August, 1988.

U.S. EPA. 1986. *Quality Criteria for Water.* EPA 440/5-86-001.

TRICHLOROETHYLENE

Use

Trichloroethylene (TCE) is a synthetic chlorinated hydrocarbon that is colorless, nonflammable, and noncorrosive. Its odor is similar to that of other chlorinated solvents used commercially (Sittig, 1991). TCE is mainly used as a metal degreaser but is also used to decaffeinate coffee, as a dry cleaning agent, and as an intermediate in the production of pesticides, paints and varnishes. TCE is moderately volatile and is used nationwide. As a result, TCE is present at a large number of hazardous waste sites. Approximately 3 percent of drinking water supplies derived from well water contain TCE at levels higher than 0.5 µg/L (EPA, 1985).

Chemical and Physical Properties

Chemical Formula: C_2HCl_3

MW: 131.5
SG: 1.464 at 20°C
FP: none
Sol. (water): 1000 mg/l
BP: 87°C
MP: -73°C
VP: 4.53 mmHg at 25°C
Sol. (organics): soluble in alcohol, ether, acetone and chloroform

Fate and Transport

The main avenues of TCE release to the environment are through the metal degreasing industry. The majority of the releases occur through volatilization, with a smaller percentage released as a result of accidental spills (EPA, 1985). Large quantities of spent TCE that were regularly landfilled are now reclaimed, eliminating that avenue of release.

TCE volatilizes from surface waters and soils and is rapidly degraded in the air. In moist soil and ground water, TCE is known to be stable, often remaining therein for a period of months to years (EPA, 1985). TCE usually degrades to either 1,2 dichloroethylene, or vinyl chloride and is a degradation product of tetrachloroethylene.

The major avenue of TCE contamination to humans is through the ground water. TCE does not bioaccumulate in animals or food chains (EPA, 1985).

Pharmacokinetics

When 200 mg/kg of ^{14}C-TCE in corn oil was administered to rats in their food, 97 percent of the dose was recovered during the 72 hours after dosing (EPA, 1985). Rats exposed to TCE by gavage at doses of 0, 10, 100 or 1,000 mg/kg/day, 5 days per week for six weeks, showed marginal increases in TCE tissue levels at the 10 mg/kg/day and 100 mg/kg/day dose groups. Compared to controls, a marked increase in TCE levels in most tissues was observed in the highest dose group. TCE was distributed throughout all tissues examined with the highest

concentrations in the fat, kidney, lung, adrenal, vas deferens, epididymis, brain and liver (EPA, 1985). Studies indicate that TCE is metabolized to trichloroethylene oxide, trichloroacetaldehye, trichloroacetic acid, monochloroacetic acid, trichloroethanol, and trichloroethanol glucuronide (EPA, 1985). Trichloroethylene and its metabolites are excreted in urine, by exhalation, and to a lesser degree in sweat, feces, and saliva (EPA, 1985).

Human Toxicity

Noncarcinogenic Effects

Systemic Effects

The National Cancer Institute (NCI) exposed Osborne-Mendel rats and B6C3F1 mice to TCE by gavage. Doses ranged between 300 and 550 mg/kg/day for mice and between 471 and 949 mg/kg/day for rats. Toxic nephropathy was observed at all dose levels.

Oral exposure of humans to 15 to 25 ml TCE resulted in vomiting and abdominal pain followed by transient unconsciousness (EPA, 1985). In a study done in 1971 by Lachnit, humans showed symptoms indicating damage to the liver parenchyma.

Teratogenic and Other Developmental Effects

The U.S. EPA reports a high rate of miscarriages among women exposed to TCE in the workplace, as noted in one case study. Swiss-Webster mice and Sprague-Dawley rats exposed to TCE vapors at a concentration of 300 ppm for 7 hours per day on days 6-15 of gestation showed no treatment-related increases in malformations. However, slightly reduced fetal body weight, delayed skeletal development, and an increase in the incidence of undescended testes were observed in mice (EPA, 1988). The offspring of pregnant rabbits exposed to TCE vapors at 500 ppm for 7 hours per day, 5 days per week beginning three weeks prior to mating on days 0-21 of gestation, or on days 6-21 of gestation, were all reported to have an increased incidence of external hydrocephalus (EPA, 1984).

Mutagenic Effects

TCE is mutagenic in *Salmonella typhimurium* and in the *E. coli* K-12 strain when liver microsomes were used for activation (EPA, 1985).

Carcinogenic Effects

TCE has been shown to be carcinogenic in different strains of mice via inhalation as well as oral exposure. The National Cancer Institute (1976) and the National Toxicology Program (1982) conducted two separate studies with TCE contaminated

with epichlorohydrin and with TCE free of epichlorohydrin. In these studies, B6C3F1 mice displayed a significant increase in liver neoplasms. Technical TCE (with epichlorohydrin and other compounds) was found to induce a hepatocellular carcinogenic response in mice. In this study, "time-weighted" average doses of 1,169 and 2,339 mg/kg for males and 869 and 1,783 mg/kg for females were administered (EPA, 1985).

Only one human study is available that shows a causative effect between TCE and human cancers. Workers were exposed to tetrachloroethylene and carbon tetrachloride in conjunction with the TCE. All other studies were inconclusive (EPA, 1984).

Ecotoxicity

Fathead minnows (*Pimephales promelas)* exposed to TCE in flow-through tests with measured concentrations and in static tests without measured exposure concentrations yielded LC_{50} (median lethal concentrations) values of 40,700 and 66,800 µg/liter, respectively. Also examined in static tests for 96 hours was the bluegill (*Lepomis macrochirus*), with an LC_{50} value of 44,700 µg/liter (EPA, 1980). The 48-hour EC_{50} (median effective concentration) value for *Daphnia magna* and TCE is 85,200 µg/L. Comparisons made among three laboratories show the 50 percent effect concentrations for *Daphnia magna* ranged from 41,000 to 100,000 µg/liter. At one laboratory, *Daphnia pulex* was also tested to determine any sensitivity, and the results were 39,000 and 51,000 µg/liter indicating no difference in sensitivity between species (EPA, 1980). TCE is practically nontoxic for freshwater aquatic organisms under these acute exposure conditions.

Standards, Criteria and Guidelines

EPA Class B2-C Carcinogen

Oral Slope Factor:	1.1×10^{-2} $(mg/kg/day)^{-1}$
Chronic Oral RfD:	6.0×10^{-3} mg/kg/day
Subchronic Oral RfD:	6.0×10^{-3} mg/kg/day
MCL:	0.005 mg/L

BIBLIOGRAPHY

Lachnit, U. Halogenated Hydrocarbons and the Liver, *Wein. Klin. Wochenschr.* 83(41): 734. 1971, (Cited in EPA, 1985).

Maltoni, C. et al. Experimental research on trichloroethylene carcinogenesis. *Arch. Res. Industrial Carcinogenesis Series,* C. Maltoni and M.A. Mehlman, Ed. Vol. V. Princeton Scientific Publishing Co., Inc., Princeton, NJ p. 393, 1986, (Cited in HEAST).

NCI (National Cancer Institute), Carcinogenesis Bioassay of Trichloroethylene, U.S. Department of Health, Education and Welfare, Public Health Service, CAS No. 79-01-6, February, 1976, (Cited in EPA, 1985).

NCI (National Cancer Institute), Bioassay of Trichloroethylene, *NCI Carcinogenesis Tech. Rep. Ser. No. 2*, 197 p., 1976, (Cited in EPA, 1988).

NIOSH, *Hazardous Waste Handbook for Health and Safety,* 1987.

NTP (National Toxicology Program), Carcinogenesis Bioassay for Trichloroethylene, CAS No. 79-01-6, No. 82-1799, (Draft), 1982, (Cited in EPA, 1985).

U.S. EPA, *Ambient Drinking Water Quality Criteria Documents,* 45FR79318, November 28, 1980.

U.S. EPA, *Drinking Water Regulations and Health Advisories.*

U.S. EPA, OERR. *CERCLA Compliance With Other Laws Manual Interim Final.* August, 1988.

U.S. EPA, Office of Drinking Water; *Health Advisory for Trichloroethylene,* 1985.

U.S. EPA, Office of Emergency and Remedial Response, *Health Effects Assessment Documents*, EPA 540/1-86/046, 1984.

U.S. EPA, *Health Effects Assessment Summary Tables (HEAST).* FY1991.

U.S. EPA, *Integrated Risk Information System (IRIS).*

VINYL CHLORIDE

Use

Vinyl chloride is used in the manufacture of polyvinyl chloride (PVC), rubber, glass, electrical wire, and automotive parts (EPA, 1985). Generally used in its gaseous state, vinyl chloride and PVC copolymers are distributed and processed as dry resins, plastisol and latex (EPA, 1985). Environmental releases of vinyl chloride generally occur where it is produced because the industrial processes in which vinyl chloride are used are consumptive (EPA, 1985).

Chemical and Physical Properties

Chemical Formula:	CH_2CHCl		
MW:	62.5	MP:	-13.37°C
SG:	0.9106 at 20°C	BP:	-153.8°C
Sol.(Water):	1,100 mg/l at 25°C	VP:	2,660 mmHg at 25°C
Sol.(Organics):	Alcohol, ether, carbon tetrachloride		

Fate and Transport

When released to surface waters, vinyl chloride volatilizes to the atmosphere within a few hours where it chemically degrades. In the atmosphere, vinyl chloride degrades within one or two days of its release. Degradation products include hydrogen chloride, formyl chloride and carbon monoxide (ICF, 1985). When released to the ground, vinyl chloride does not adsorb to soils and leaches readily to the ground water.

In the ground water, vinyl chloride may degrade to carbon dioxide and the chloride ion (EPA, 1985). Ground water is considered to be the major source of human exposure to vinyl chloride (EPA, 1985).

Pharmacokinetics

Vinyl chloride is absorbed rapidly in rats exposed via inhalation and ingestion. The greatest concentration of absorbed vinyl chloride was found in the liver, kidneys, muscle, lungs, fat, spleen, and brain of rats following exposure via inhalation and ingestion (EPA, 1985). Hefner et al. (1975) noted that vinyl chloride is metabolized primarily by alcohol dehydrogenase. After absorption into the body, vinyl chloride and its metabolites are excreted in the urine.

Human Toxicity

Noncarcinogenic Effects

Systemic Effects

Vinyl chloride is known to be hepatotoxic to workers exposed in the PVC manufacturing business (ACGIH 1984). One study reported that acute exposure to high levels of vinyl chloride causes central nervous system dysfunction such as euphoria, dizziness, and incoordination (ACGIH, 1984). Chronic exposure to high concentrations of vinyl chloride is known to cause bronchitis, headache, irritability, and severe systemic disorders such as sclerotic syndrome, acro-osteolysis, thrombocytopenia, and liver damage (ICF, 1985). Liver damage appeared to be the most abundant systemic effect of chronic exposure in laboratory animals. In another study, researchers exposed rats to 30,000 ppm vinyl chloride for 4 hours/day, 5 days/week in an attempt to induce acro-osteolysis, a condition described as a combination of thrombopenia, liver damage, circulatory obstruction, and bone alterations. Metaplastic bone changes, similar to those noted in cases of acro-osteolysis in humans, were noted in this study (ACGIH, 1984).

Teratogenic and Other Developmental Effects

Minor skeletal abnormalities and an increased fetal death rate was noted in experimental animals exposed to vinyl chloride via inhalation (ICF, 1985). In humans, a significant increase in fetal deaths was noted in women whose husbands were occupationally exposed to vinyl chloride (ICF, 1985).

Mutagenic

Vinyl chloride appears to be mutagenic to bacteria and fruit flies (EPA, 1985). Abundant chromosomal aberrations were noted in occupationally exposed workers (ICF, 1985).

Carcinogenic Effects

Vinyl chloride is classified as a known human and animal carcinogen (Class A) by the International Agency for Research and Cancer (IARC). IARC found that chronic, occupational exposure to vinyl chloride causes an increase in the number of liver angiosarcomas, brain tumors, lung tumors, hemopoietic tumors, and lymphopoietic tumors (EPA, 1985).

Feron et al. (1981) administered, via ingestion, 1.7 mg vinyl chloride/kg bw/day, to rats over their lifespan. The treatment induced an increase in angiosarcomas, hepatocellular carcinomas, and adverse hepatic effects. Maltoni (1981) noted that

chronic inhalation of vinyl chloride by rats and mice induced liver cancer and tumors in various other bodily tissues.

Ecotoxicity

Pertinent information regarding the ecotoxic effects of vinyl chloride were not located in the available literature although, it can be inferred from the effects on laboratory animals, that vinyl chloride is highly toxic to most organisms.

Standards, Criteria and Guidelines

EPA Class A Carcinogen

Oral Slope Factor:	1.9×10^{0} $(mg/kg/day)^{-1}$
Chronic Oral RfD:	NA
Subchronic Oral RfD:	NA
MCL:	0.002 mg/L

BIBLIOGRAPHY

American Conference of Governmental Industrial Hygienists; *Documentations of the Threshold Limit Values,* 1984.

Feron, V.J., C.F.M. Hendrikson, A.J. Speek, H.P. Til and B.J. Spit, Lifespan and Toxicity Study of Vinyl Chloride in Rats, 1981, *Fd. Cosmet. Toxicol.*, 19: 317-331, (Cited in EPA, 1985).

Hefner, R.E., Jr., P.G. Watanabe and P.J. Gehring. Preliminary Studies on the Fate of Inhaled Vinyl Chloride Monomer in Rats, 1975, *Ann. N. Y. Acad. Sci.*, 2461 135-148, (Cited in EPA, 1985).

Maltoni, C., G. Lefemine, A. Ciliberti, G. Cotti and D. Caretti. Carcinogenicity bioassays of Vinyl Chloride Monomer: A Model of Risk Assessment on an Experimental Basis, 1981. *Environ. Health Perspec.*, 41: 3-31, (Cited in EPA, 1985).

Sittig, Marshall, *Handbook of Toxic and Hazardous Chemicals,* 1991.

U.S. EPA, *Drinking Water Regulations and Health Advisories.*

U.S. EPA, *Health Advisory for Vinyl Chloride,* 1985.

U.S. EPA, *Health Effects Assessment Summary Tables (HEAST).* FY1991.

U.S. EPA, OERR. *CERCLA Compliance With Other Laws Manual Interim Final.* August, 1988.

U.S. EPA, *Quality Criteria for Water,* EPA 440/5-86-001. May 1986.

BASE-NEUTRAL/ACID EXTRACTABLES

BIS(2-ETHYLHEXYL)PHTHALATE

Use

The phthalate esters, such as bis(2-ethylhexyl)phthalate (BEHP), are widely used in PVC resins and vinyl copolymer resins to impart flexibility to the finished product. Other reported uses include as an inert ingredient in pesticides, a component in dielectric fluids (replacing PCBs) in electric capacitors, a solvent for erasable ink, acarid in orchids, in vacuum pump oils, and as a testing agent for air filtration systems. Consumer products using BEHP include vinyl upholstery, table cloths, shower curtains, raincoats, and food wrap. Annual consumption of BEHP is approximately 130 million kg.

Chemical and Physical Properties

Chemical Formula: C_6H_{40} $(COOCH_2CH$ $(C_2H_5)C_4Hg)_2$

MW:	3,190	BP:	386.9 C at 5 mmHg
SG:	0.985 at 20 C	MP:	-50 C
FP:	218.33 C	VP:	2×10^{-7} mmHg at 20 C

Sol. (water): 0.4 mg/L at 25 C
Sol. (organics): mineral oil and hexane

Fate and Transport

In aquatic media, BEHP does not volatilize or photo-oxidize readily. Apparently, adsorption to suspended solid and particular matter are probably the most important of BEHPs fate processes (ICF, 1985). Bioaccumulation is another important fate process for BEHP. Several unicellular and multicellular aquatic organisms are known to accumulate BEHP (ICF, 1985).

In soils, BEHP would be expected to sorb to organic matter. Very little volatilization and leaching would be expected (ICF, 1985).

Pharmacokinetics

Studies indicate that, following an oral dose, BEHP is initially hydrorolyzed by a nonspecific lipase in the gastrointestinal tract to produce mono(ethylhexyl)phthalate (MEHP) (and 2-ethylhexanol) which is readily absorbed from the gastrointestinal tract. One study indicated that BEHP is poorly absorbed following dermal application. In acute inhalation toxicity studies in rats, it has been demonstrated that BEHP is absorbed by the lung. Information on the oral absorption of BEHP in humans is limited, and data is not available on the absorption of BEHP by humans exposed via inhalation or through dermal exposure (ATSDR, 1989).

Absorbed BEHP and is metabolites are distributed rapidly to tissues and organs with only a slight cumulative potential. The liver appears to be the major, initial repository organ. BEHP is eliminated from the body mainly through urinary excretion. Urinary metabolites appear to differ amongst species (ATSDR, 1989).

Human Toxicity

Noncarcinogenic Effects

Systemic Effects

Various rodent studies revealed LD_{50}s ranging from 26,000 to 49,000 mg/kg following oral exposure. No data are available on the effects of oral, ingestion, or dermal exposure to BEHP on lethality in humans (ATSDR, 1989).

The liver and the testes have been shown to be the primary target organs of BEHP. Morphological and biochemical changes in the liver of exposed rodents have been observed following exposure to high doses of BEHP. No data are available on the hepatic toxicity of BEHP in humans via inhalation, oral, or dermal exposure. Testicular effects, including a decrease in relative organ weight and histological changes in the seminiferous tubules have been observed in the rat and mouse, but not in the hamster, ferret, or marmoset following exposure to BEHP and MEHP (ATSDR, 1989).

Teratogenic and Other Developmental Effects

BEHP is a reproductive toxicant in male and female mice; reduced fertility and both production of fewer litters by breeding pairs and decreased litter size has been observed (ATSDR, 1989). Available data suggests that BEHP is developmentally toxic in rats and mice. One study indicated that, following administration of 0.05, 0.1, 1.0, 2.5, 5.0, or 10.0 Ml/kg BEHP by gavage on day 7 of gestation, a decrease in body weight of live fetuses occurred at the 0.05 mL/kg dose. At doses administered at or above 0.1, mL/kg, a decrease in fetal body weight was observed, and the fetuses were deformed or dead. In a study in which pregnant Fisher 344 rats were exposed to BEHP in their diets during 0 to 20 of gestation, the number and percentage or resorptions, non-live fetuses, and malformed fetuses were increased in a dose-related manner; with a statistically significant increase in the high-dose group (20,000 ppm/1,055 mg/kg/day) (ATSDR, 1989). The NOAEL for teratogenic effects or maternal toxicity in a study of pregnant CD-1 mice exposed to BEHP in their diets was 250 ppm. BEHP was found to be developmentally toxic in ICR mice when administered orally (at 1,000 mg/kg and 2,000 mg/kg), but not when administered by intraperitoneal injection. One hundred percent of live fetuses were malformed when pregnant mice were given 1 mL/kg MEHP on day 8 of gestation (ATSDR, 1989).

Mutagenic Effects

BEHP has not been shown to be mutagenic in most microbial and mammalian assay systems. Most of the data also suggest that MEHP and 2-ethylhexanol are not mutagenic (ATSDR, 1989).

Carcinogenic Effects

EPA has evaluated the weight of evidence on the carcinogenicity of BEHP and has concluded that it is a probable human carcinogen (Group B2). Evidence on potential carcinogenicity from animal studies is "sufficient", however there is no adequate human data. Data from a bioassay using Fisher 344 rats and B6C3F1 mice have been used by EPA to calculate the upper-bound incremental unit carcinogenic risk to humans (the unit risk value is estimated to be 4.0×10^{-7} for drinking water containing 1 µg/L BEHP). These rodents were fed diets containing 0, 6,000 or 12,000 ppm for 103 weeks. A statistically significant increase in hepatocellular carcinomas and neoplastic nodules was observed in the high dose groups (NTP, 1982).

Ecotoxicity

The LC_{50} values for the midge, scud, and bluegill all exceeded the highest concentrations tested, which were 18,000 32,000 and 770,000 µg/liter, respectively. Because these values are greater than the water solubility of the chemical, it is unlikely that BEHP will be acutely toxic to organisms in natural waters. In a chronic toxicity test with *Daphnia magna,* significant reproductive impairment was found at the lowest concentration tested, 3µg/liter. These data imply that some chronic toxicity will be observed in freshwater aquatic life subsequent to long-term exposure to BEHP (ICF, 1985).

BEHP is removed from water primarily through uptake by suspended matter, sediments, and biota. BEHP is absorbed by both single- and multi-cellular organisms. The tendency for BEHP to undergo bioaccumulation is lessened because it is degraded by microorganisms and metabolized by invertebrates, fish and other animals. Very rapid bioaccumulation and concentration factors ranging from several hundred to several thousand times the concentration of BEHP in water, however, have been observed for various aquatic organisms, seen mostly in smaller aquatic invertebrates (ATSDR, 1989).

Acute and chronic toxicity to freshwater aquatic life occurs at concentrations as low as 940 and 3 µg/L, respectively, according to available data; more sensitive species than those tested would be expected to be affected by even lower concentrations. For saltwater aquatic life, acute toxicity occurs at concentrations as low as 2,944 µg/L. No data are available to enumerate the chronic toxicity of phthalate esters to saltwater aquatic life; however, toxicity of one species of algae occurs at concentrations as low as 3.4 µg/L (EPA, 1986).

Standards, Criteria and Guidelines

EPA Class B2 Carcinogen

Oral Slope Factor:	1.4×10^{-2} $(mg/kg/day)^{-1}$
Chronic Oral RfD:	2×10^{-2} mg/kg/day
Subchronic Oral RfD:	2×10^{-2} mg/kg/day
MCL:	0.006 mg/L

AWQC: Acute: 400 µg/L (proposed)
Chronic: 360 µg/L (proposed)

BIBLIOGRAPHY

Agency for Toxic Substances and Disease Registry. U.S. Public Health Service. 1989. *Toxicological Profile for di(2-ethylhexyl)phthalate,* ATSDR/TP-88/15.

Carpenter, C.P., et. al. 1953. Chronic oral toxicity of di(2-ethylhexyl) phthalate for rats and guinea pigs. *Arch. Indust. Hyg. Occup. Med.* 8: 219-226. (Cited in IRIS).

Carpenter, C.P., et. al. 1953. Chronic oral toxicity of di(2-ethylhexyl) phthalate for rats, guinea pigs, and dogs. *AMA Arch. Ind. Hyg. Occup. Med.* 8:219-226. (cited in IRIS).

ICF Clement Associates. 1985. *Chemical, Physical and Biological Properties of Compounds Present at Hazardous Waste Sites,* Final Report.

National Toxicity Program (NTP). 1982. Carcinogenesis bioassay of bis-(2-ethylhexyl) phthalate (CAS No. 1117-81-7) in F344 rats and B6C3F1 mice (feed study). *NTP Tech. Rep. Ser. Tr. No. 217,* NTP, Research Triangle Park, NC. (Cited in IRIS).

U.S. EPA. *Drinking Water Regulations and Health Advisories.*

U.S. EPA. *Integrated Risk Information System (IRIS).*

U.S. EPA. *Health Effects Assessment Summary Tables (HEAST).*

U.S. EPA, OERR. *CERCLA Compliance With Other Laws Manual Interim Final.* August, 1988.

U.S. EPA. 1986. *Quality Criteria for Water,* EPA 440/5-86-001.

POLYCYCLIC AROMATIC HYDROCARBONS

Background

Polycyclic Aromatic Hydrocarbons (PAHs) constitute a class of materials which are characterized as containing more than one benzene ring. Because of the similarities between them, PAHs have been summarized in one toxicity profile. Discussions of specific PAHs are provided in cases where available literature exists. Otherwise, PAHs are discussed in general terms. The most common and the most hazardous PAH is benzo (a) pyrene (BaP). As a result, most of the information located in the available literature deals with BaP.

Use

As a class, PAHs are used industrially in the production of automobile tires, rubber stoppers, dyes, and glass and can be found in yeasts, whiskeys, dried prunes, and cigarette smoke (ICF, 1985). PAHs are often found as byproducts to the refining processes of petroleum, shale, coal, and coke.

Chemical and Physical Properties

Summarized in Table 1.

Fate and Transport

In general, PAHs are expected to exist as vapor and particulates in the atmosphere. Once in the atmosphere, PAHs may be removed through photochemical reactions, chemical reactions, or by wet and dry deposition. In aquatic media, PAHs are expected to volatilize, react photochemically, and be degraded microbially. In high water and wind flow conditions, volatilization would occur readily. In water, PAHs would adsorb to organic matter and would most likely fall out of the water column (EPA, 1984a).

In soils, PAHs are subject to microbial degradation and adsorption. Because of their affinity to organic matter, PAHs are not expected to be highly mobile in soils, therefore, leaching to ground water is not considered to be a significant fate process.

Pharmacokinetics

Although few studies have been performed on human ingestion of PAHs, it is thought that they would be absorbed readily in the gastrointestinal tract. Benzo (a) pyrene (BaP), chrysene, and benzo (a) anthracene (BaA), three of the more common PAHs, are reported to transport passively across the gastrointestinal mucosa (EPA, 1984a). Chang (1943) noted that rats given BaP by gavage absorbed approximately 50 percent of the administered dose. Certain PAHs require metabolic activation by specific enzymatic systems in order to acquire carcinogenic properties. PAHs and their metabolites are excreted through the feces and through the hepatobiliary system. There is little evidence that PAHs bioaccumulate extensively (EPA, 1984a).

Human Toxicity

Acenapthene

Knobloch, et al. (1969) reported that, when administered orally to rats, acenapthene causes changes in renal function, lowers body weight and causes unspecified changes in the peripheral vascular system (EPA, 1984f). Mild morphological damage to the kidneys and liver were also noted. U.S. EPA (1989a) reports liver weight changes accompanied by microscopic alterations in mid- to high-dose mice exposed to acenapthene ranging in concentration form 0 to 700 mg/kg/day. Nonspecific pneumonia was noted by Reshetyuk et al. (1970) in rats exposed to 12 mg/m^3 acenapthene by inhalation for 4 hours/day, 6 days/week for 5 months (EPA, 1984f).

Acenapthene has not been shown to be mutagenic; however, it is known to cause changes in the DNA content of a number of plant and microbial species. These changes are a result of disruptions of the spindle mechanisms during mitosis (ICF, 1985).

At high exposure levels, acenapthene is known to cause liver and kidney damage, but is not known to be carcinogenic (ICF, 1985).

Acenaphthylene

The U.S. EPA is currently reviewing the noncarcinogenic risk assessment of this substance (IRIS). No data relative to the toxicity of this chemical were found in the literature reviewed.

Kaden et al. (1979) found that acenaphthylene (1mM) yielded positive results in a *Salmonella typhimurium* forward mutation assay. However, Bos et al. (1988) reported negative results in *S. typhimurium* strains TA98 and TA100 in the presence of hepatic homogenates.

Cook (1932) observed no carcinogenic effect in a lifetime study of the effect of dermally introduced 0.25 percent acenaphthylene in mice. Survival, however, was only 65 percent at 6 months and 35 percent at 12 months.

Anthracene

Chronic exposure to anthracene is thought to cause dermatitis, hyperkeratoses, and other skin disorders in workers (ICF, 1985). Numerous studies of chronic and acute exposure of laboratory animals to anthracene have suggested that it does not cause any systemic toxic effects (i.e., U.S. EPA, 1989b).

Anthracene has been shown to cause reproductive effects in mice given a single oral dose during the last week of gestation. A lower survival rate was seen in experimental mice than in controls (IARC, 1983).

In twenty experiments on the mutagenicity of anthracene, very few have resulted in positive effects (IARC, 1983); therefore, not enough evidence is available to consider anthracene a mutagen. There are no epidemiologic studies available that suggest anthracene is carcinogenic to humans. In studies of the effects of subcutaneous injections of anthracene to laboratory animals, it was noted to cause local tumors. The carcinogenic effects of subcutaneous injections of anthracene appear to be enhanced by ultra-violet light. Schmahl (1955), however, found no incidence of tumors following exposure of rats to 4.5 g anthracene/rat over 78 weeks.

However, this evidence was determined to be inadequate in proving anthracene's carcinogenicity (IARC, 1983).

Benzo (a) Anthracene

Benzo (a) anthracene (BaA) is known to cause skin disorders, such as hyperplasia and hyperkeratosis, in workers exposed occupationally (ICF, 1985). Cutaneous exposure to BaA causes destruction of the sebaceous glands of laboratory mice and, when injected repeatedly, BaA produces gross changes in the lymphoid tissues of mice and rats (ICF, 1985).

It is also known that many carcinogenic PAHs, such as BaA, cause immunosuppressive effects, although studies on BaA have not been conclusive (ICF, 1985).

BaA is known to be mutagenic in *Salmonella typhimurium* and *Drosophila melanogaster.* It is also known to cause sister-chromatid-exchange in cultured mammalian cells.

Several studies indicate that BaA is carcinogenic to laboratory animals. Oral administrations and sub-cutaneous injections have resulted in statistically significant increases in tumors and adenomas (Klein, 1963; IARC, 1983).

Benzo (a) Pyrene

From laboratory studies performed on mice, it appears as though BaP's toxicity to organisms is dependent upon the constitution of a specific gene locus. The particular locus determines whether or not aryl-hydrocarbon-hydroxylase, an enzyme which alters the chemical makeup of aromatic hydrocarbons, is easily released (induced) into the body (EPA, 1985). Those animals that cannot easily induce the release of aryl hydrocarbon hydroxylase are more susceptible to BaP's toxic effects. Robinson, et al. (1975) administered 120 mg/kg-bw BaP in food to "poorly inducible" and "easily inducible" mice. The "poorly inducible" mice developed aplastic anemia and died within 4 weeks whereas the "easily inducible" mice remained healthy for at least 6 months.

In a study a carried out by Rigdon and Rennels (1964), only one of seven pregnant female rats carried viable fetuses to term, after having been fed a diet containing BaP

at a level of 50 mg/kg/day for up to 3.5 months. Of four pups delivered, two were stillborn, one of which was grossly malformed. A third was killed for observational purposes, while the fourth died of starvation because it did not appear to be lactating.

In a teratogenicity and reproduction study, Rigdon and Neal (1965) fed diets containing BaP at a level of 0, 250, 500, or 1,000 mg/kg to male and female mice over various time spans during mating, gestation, and lactation. No apparent reproductive, teratogenic, embryotoxic or fetotoxic effects were observed.

MacKenzie and Angevine (1981) administered BaP orally at a level of 10 mg/kg/bw to CD-1 mice during pregnancy. There was no effect on fetal body weight; however, reduced fertility and reproductive capacity were observed in the offspring.
BaP has been used as a positive control in a variety of short-term tests. It has yielded positive results in assays for bacterial mutation, mutation in *Drosophila melanogaster*; DNA binding, DNA repair, sister chromatid exchange (SCE), chromosomal aberration, point mutation and transformation in mammalian cells in culture; and *in vivo*, including DNA binding, SCE, chromosomal aberration, sperm abnormality and the specific locus (spot) test (IARC, 1982; deSerres and Ashby, 1981; Hollstein and McCann, 1979).

PAH mixtures containing BaP have been shown to induce lung cancer in humans as a result of chronic exposure to cigarette smoke, roofing tar, and coke oven emissions (IRIS). It is impossible to conclude from these studies however, that BaP is the responsible agent.

Cottini and Mazzone (1939) applied a 1 percent solution of BaP to the skin of 26 patients. The skin of the patients developed regressive verrucae, reversible and apparently benign cysts that are thought to represent the early stages of neoplasia.

BaP is known to be carcinogenic to mice when exposed subcutaneously. Neal and Rigdon (1967) noted a dose-response relationship in the incidence of stomach tumors in male and female CFW-Swiss mice treated orally with 1-250 ppm BaP for 197 days. Individuals treated with greater than 20 ppm doses exhibited a significant increase in stomach carcinomas and papillomas. Mice treated with 250 ppm BaP exhibited an increase in the incidence of lung adenoma and leukemia.

In an inhalation study, Thyssen, et al. (1981) exposed hamsters to 2.2, 9.5 or 45 mg/m^3 BaP for 4.5 hours/day for 10 weeks and 3 hours/day 7 days/week for up to 675 days. Animals exposed to 9.5 mg/m^3 developed tumors of the nasal cavity, larynx trachea and pharynx. Animals exposed to 45 mg/m^3 BaP developed a significant number of tumors in the respiratory tract and upper digestive tract.

Benzo (b) Fluoranthene

No data concerning the systemic effects of benzo (b) fluoranthene (BbF) on humans or laboratory animals were located in the available literature.

One study has demonstrated that BbF caused chromosomal aberrations in the bone-marrow cells of Chinese hamsters (IARC, 1983). In this study, hamsters were given two doses of 450 mg BbF/kg-bw. In separate studies, unspecified mutations in *Salmonella typhimurium* cultures were noted when exposed to 100 µg BbF (IARC, 1983).

BbF is known to be carcinogenic to laboratory mice and rats. 3-month old female Osborne-Mendel rats exposed to BbF through lung implants illustrated a dose-related increase in the incidence of epidermoid carcinoma and pleomorphic sarcomas in the lung and thorax (Deutsch-Wenzel et al., 1983). A 0.5 percent solution of BbF produced papilloma in 100 percent of laboratory mice that were painted three times per week (IARC, 1983). In one study, researchers were able to induce local sarcoma in 18 of 24 mice that were subcutaneously injected with 0.6 mg BbF. The lowest carcinogenic dose of BbF painted on mice was noted to be a 0.01 percent solution (IARC, 1983).

No experiments concerning the carcinogenic effects of BbF on humans were located in the available literature.

Benzo (k) Fluoranthene

No data concerning the systemic effects of benzo (k) fluoranthene (BkF) on humans or laboratory animals were located in the available literature. BkF was reported to be mutagenic in bacteria such as *Salmonella typhimurium* (IARC, 1983).

The International Agency for Research on Cancer (IARC) has determined that there is sufficient evidence to prove that BkF is carcinogenic to laboratory animals. Tumors were noted in 69 percent of NMRI mice treated with 9.2 mg BkF/kg-bw. In this study, 3.4, 5.6 or 9.2 mg BkF were applied to the mice's skin. In the lowest test group, 8 of 34 individuals exhibited local tumors (IARC, 1983).

When injected into the pulmonary tissues of rats, BkF caused squamous cell carcinomas (IARC, 1983). Female Osborne-Mendel rats exposed to BkF through lung implants illustrated a dose-related increase in the incidence of epidermoid carcinomas in the lung and thorax (Deutsch-Wenzel, et. al., 1983).

Benzo (g,h,i) Perylene

No data concerning the systemic effects of benzo (g,h,i) perylene (B(g,h,i)P) on humans or laboratory animals were located in the available literature. IARC states that

there is inadequate evidence to prove that B(g,h,i)P is toxic when exposure is short-term.

B(g,h,i)P was shown to be mutagenic to *Salmonella typhimurium* when administered in various doses (IARC, 1983).

In seven studies evaluated by IARC, B(g,h,i)P caused no visible carcinogenic effects. The tests included five skin application assays, one intrapulmonary injection study, and one co-administration study. In the latter study, B(g,h,i)P was administered with BaP. A higher number of skin tumors was noted in the test group than in the group administered BaP alone (IARC, 1983).

There is not sufficient evidence to classify B(g,h,i)P as carcinogenic to humans or laboratory animals (IARC, 1983).

Chrysene

Chrysene's toxic effects to humans and animals have not been studied extensively. It is expected that chrysene causes damage to epidermal tissues in workers exposed daily. Although not specific to chrysene, numerous studies indicate that PAHs cause immunorepressive effects (IARC, 1983).

Chrysene was shown to be mutagenic to *Salmonella typhimurium* when administered at doses of 10 mg/plate. Another study concluded that chrysene causes embryonic cell transformations in Syrian hamsters. Chrysene is known to cause sister-chromatid-exchange in Chinese hamsters and aberrations in the oocyte development of laboratory mice (IARC, 1983).

Chrysene is thought to be weakly carcinogenic to laboratory animals. It does not appear to be locally or systemically carcinogenic to laboratory animals when exposed epidermally although some studies provide evidence to the contrary. A number of these studies were ignored due to contamination to stock by methylchrysenes (IARC, 1983). Perinatal and subcutaneous administrations have resulted in similar effects and conclusions.

Although some studies have indicated chrysene to be carcinogenic to laboratory animals (Wislocki et al., 1986), IARC has determined that only limited evidence of chrysene's carcinogenicity exists.

Dibenzo (a,h) Anthracene

Researchers reported a decreased growth rate in young rats when exposed to between 3 and 90 mg/kg bw dibenzo (a,h) anthracene (D(a,h)A), (IARC, 1983). No other evidence of systemic or local noncarcinogenic toxic effects were located in the available literature.D(a,h)A was found to be mutagenic to a number of cultured and *in*

vivo cells. D(a,h)A was highly mutagenic to *Salmonella typhimurium.* It also induced unscheduled DNA syntheses in the presence of an exogenous metabolic system in cultured mammalian cells. D(a,h)A was found to be embryotoxic to rats when administered in high doses (IARC, 1983).

D(a,h)A has produced tumors in rats, guinea pigs, mice, frogs, pigeons, and chickens (Snell and Stewart; 1962, 1963). Carcinogenic affects, both local and systemic, have been noted as a result of oral, intratracheal, and cutaneous applications (IARC, 1983).

Fluoranthene

Male and female CD-1 mice (20/sex/group) were exposed to 0, 125, 250, or 500 mg/kg/day fluoranthene by gavage for 13 weeks (U.S. EPA, 1988a). Mice exhibited increased food consumption and body weight gain at the highest dose. Increased SGPT values and increased absolute and relative liver weights occurred at 250 and 500 mg/kg/day. Compound-related microscopic liver lesions were observed in 65 and 87.5 percent of the mid- and high-dose mice, respectively.

Fluoranthene was found to be mutagenic in *Salmonella typhimurium* and *in vitro* human lymphoblastoid cells in the presence of an exogenous metabolic system (IARC, 1983). There have been no studies done that indicate fluoranthene to be carcinogenic to humans or laboratory animals. Of eight studies reviewed by IARC, none provided sufficient evidence to conclude that fluoranthene is carcinogenic. However, one study noted twice as many tumors in mice administered fluoranthene in conjunction with BaP than in mice administered BaP alone (IARC, 1983).

Fluorene

CD-1 mice (25/sex/group) were exposed to 0, 125, 250, or 500 mg/kg/day fluorene by gavage for 13 weeks (U.S. EPA, 1989c). Increased spleen, liver, and kidney weights were observed at the high doses. Other systemic effects included a decreasing trend in BUN and an increasing trend in serum bilirubin.

Fluorene does not appear to be mutagenic, teratogenic, or embryotoxic to laboratory animals. Three studies were reviewed by IARC, all were inconclusive as to the reproductive effects of fluorene (IARC, 1983).

Fluorene did not cause cancer in laboratory animals from skin applications, subcutaneous injections, or oral administrations (IARC, 1983). Due to insufficient studies, there is inadequate evidence to evaluate the carcinogenicity of fluorene (IARC, 1983).

Indeno (1,2,3-cd) Pyrene

No data regarding the systemic, mutagenic, teratogenic, or developmental effects of indeno (1,2,3-cd) pyrene (IP) were located in the available literature.

IP is carcinogenic to laboratory mice when administered by skin painting at a dose of 250 µg. Researchers noted that doses of 0.01 and 0.05 percent IP produced no tumors. A dose of 0.1 percent IP produced a total of 6 papillomas and 3 carcinomas in 20 mice. Seven papillomas and five carcinomas were noted in 20 mice painted with 0.5 percent IP. The same study demonstrated that 10 paintings at two-day intervals, resulting in a total dose of 250 mg initiated skin carcinogenesis (IARC, 1983).

When administered subcutaneously to mice, 0.6 mg IP given at one-month intervals, produced 10 sarcomas in 14 male mice and 1 sarcoma in 14 female mice (IARC, 1983).

In a lung implantation study (Deutsch-Wenzel et al., 1983), IP produced epidermoid carcinomas.

2-Methylnapthalene

No data were located in the available literature.

Naphthalene

Naphthalene appears to effect ocular function in humans, rats, and rabbits. Ghetti and Mariani (1956) reported that 8 of 21 workers exposed to an unspecified concentration of naphthalene in a dye-manufacturing process developed cataracts. All of these workers were less than 50 years of age. Fitzhugh and Buschke (1949) observed cataracts in young rats exposed to 2 percent naphthalene by ingestion for 60 days (approximately 1 g/kg bw/day). Ghetti and Mariani (1956) noted similar effects in rabbits.

Naphthalene is known to be fetotoxic because of its ability to cross the placental wall (EPA, 1984). It is also known to cause DNA damage in mice (ICF, 1985). The offspring of rats injected with unspecified amounts of naphthalene displayed retarded cranial and heart development (ICF, 1985).

Wolf (1976) reported that 6 of 15 workers exposed, via inhalation, to naphthalene develop laryngeal carcinomas and neoplasms of the pylorus and cecum. A study on the effects to rats of subcutaneously injected naphthalene concluded with negative results (Schmahl, 1955). The rats were injected with either 10 or 0.82 g naphthalene for an unspecified amount of time. No tumors were noted. (EPA, 1984b).

Phenanthrene

No data regarding the systemic effects of phenanthrene to humans or laboratory animals were located in the available literature.

The majority of the studies concerning the developmental effects of phenanthrene concluded with negative results. One study reported that *Salmonella typhimurium* mutated when exposed to 12 mg phenanthrene (IARC, 1983). Abnormally high concentrations of exogenous metabolites were introduced into the culture before mutations were seen. In two other experiments, phenanthrene was reported to induce mutations *in vitro* human cells and *in vivo* hamster cells. These studies do not provide enough evidence to classify phenanthrene as a mutagenic compound (IARC, 1983).

Experiments indicate that phenanthrene is not carcinogenic to laboratory animals (Higgins and Yang, 1962). No case studies of human exposure to phenanthrene were located. Mice and rats were exposed to phenanthrene via painting, subcutaneous injections, intraperitoneal injections, and ingestion. None of the studies resulted in the induction of tumors (IARC, 1983).

Pyrene

Cd-1 mice were exposed to 0, 75, 125, or 250 mg/kg/day pyrene by gavage for 13 weeks (U.S. EPA, 1989d). Nephropathy and reduced relative and absolute kidney weights were observed in the high dose groups.

It was noted in one study of the effects of pyrene exposure that the growth of young rats was inhibited when fed 2000 mg pyrene/kg/day for 100 days. In the same study, it was noted that the rats' livers were enlarged after prolonged exposure (IARC, 1983). No toxic effects to humans or animals resulting from pyrene exposure were noted in the available studies, although one researcher reported an LD_{50} for mice of 678 mg pyrene/kg-bw for 4 days (IARC, 1983). Pyrene induced unscheduled DNA synthesis in cultured rat hepatocytes (EPA, 1984d) and cultured human fibroblast cells (IARC, 1983). It induced sister-chromatid-exchange in Syrian hamster embryonic cells in one instance and, in another, it mutated *Salmonella typhimurium* cultures (IARC, 1983).

The carcinogenic effects of pyrene on laboratory animals have been studied extensively. Oral, inhalation, injection, and topical studies have all been performed and have all concluded that pyrene is noncarcinogenic (EPA, 1984d). Pyrene did not initiate tumors in mouse skin, although it did enhance the carcinogenic effects of benzo (a) pyrene when co-applied. Evidence regarding the carcinogenicity of intratracheal administration were considered inadequate for evaluation (IARC, 1983).

Ecotoxicity

The ecotoxic effects of PAHs have not been widely studied. It appears as though the effects of PAHs on aquatic organisms are more variable than the effects on humans.

Acenapthene resulted in 96-hour LC_{50} values of 970 and 2,230 mg/l for mysid shrimp and sheepshead minnows, respectively. Two freshwater species subjected to acenapthene exposure displayed EC_{50} values of 41,200 and 1,700 mg/l (*Daphnia magna* and bluegill, respectively) (ICF, 1985).

Fluoranthene appears to be less toxic to freshwater species than does acenapthene. The 96-hour LC_{50} value for bluegill was 3,970 mg/l and the 48-hour EC_{50} value for *Daphnia magna* was 325,000 mg/l. The 96-hour LC_{50} value for mysid shrimp, a saltwater species, was 40 mg/l, significantly lower than the value for acenapthene (ICF, 1985). Fluoranthene is known to bioaccumulate but, to what extent is unknown.

The medium effect concentration of naphthalene for freshwater species was reported to be greater than 2,300 mg/l. Acute values for saltwater species (polychaetes, oysters, shrimp) are reported to be greater than 2,350 mg/l (ICF, 1985).

Standards Criteria and Guidelines

EPA Weight of Evidence:	Benzo(a)anthracene:	B2
	Benzo(a)pyrene:	B2
	Benzo(b)fluoranthene:	B2
	Benzo(ghi)perylene:	D
	Fluoranthene:	D
	Naphthalene:	D
	Phenanthrene:	D
	Pyrene:	D
	2-Methylnaphthalene:	NA
Oral Slope Factor:	Benzo(a)anthracene:	7.30×10^{-1} $(mg/kg/day)^{-1}$
	Benzo(a)pyrene:	7.30×10^{0} $(mg/kg/day)^{-1}$
	Benzo(b)fluoranthene:	7.30×10^{-1} $(mg/kg/day)^{-1}$
	Benzo(ghi)perylene:	NA
	Fluoranthene:	NA
	Naphthalene:	NA
	Phenanthrene:	NA
	Pyrene:	NA
	2-Methylnaphthalene:	NA
Chronic Oral RfD:	Benzo(a)anthracene:	NA
	Benzo(a)pyrene:	NA
	Benzo(b)fluoranthene:	NA
	Benzo(ghi)perylene:	4.00×10^{-2} mg/kg/day

	Fluoranthene:	4.00×10^{-2} mg/kg/day
	Naphthalene:	4.00×10^{-2} mg/kg/day
	Phenanthrene:	4.00×10^{-2} mg/kg/day
	Pyrene:	4.00×10^{-2} mg/kg/day
	2-Methylnaphthalene:	NA
Subchronic Oral RfD:	Benzo(a)anthracene:	NA
	Benzo(a)pyrene:	NA
	Benzo(b)fluoranthene:	NA
	Benzo(ghi)perylene:	4.00×10^{-2} mg/kg/day
	Fluoranthene:	4.00×10^{-1} mg/kg/day
	Naphthalene:	4.00×10^{-2} mg/kg/day
	Phenanthrene:	4.00×10^{-2} mg/kg/day
	Pyrene:	3.00×10^{-2} mg/kg/day
	2-Methylnaphthalene:	NA
AWQC:	Napthalene:	Acute: 2,300 µg/L (LOEL)
		Chronic: 620 µg/L (LOEL)

BIBLIOGRAPHY

Adkins, B., et al. 1986. Oncogenic response of strain A/J mice to inhaled chemicals. *J. Toxicol. Environ. Health* 17:311-3222. (cited in IRIS).

American Conference of Governmental Industrial Hygienists. 1984. *Documentation of the Threshold Limit Values.*

Badger, G.M., et al. 1944. The production of cancer by pure hydrocarbons. *V. Proc. R. Soc. London Ser. B* 129: 439-467. (cited in IRIS).

Bos, R.P., et al. 1988. Mutagenicity of bi, tri-, and tetra-cyclic aromatic hydrocarbons in the "taped-plate assay" and in the conventional Salmonella Mutagenicity assay. *Mutat Res.* 204: 203-206. (cited in IRIS).

Chang, L.H. The fecal Excretion of Polycyclic Hydrocarbons Following Their Administration to the Rat. *J. Biol. Chem.* 151: 93-1943. (Cited in EPA, 1984a).

Clayton and Clayton. 1978. *Patty's Industrial Hygiene and Toxicology Vol. IIB.* (Patty's)

Cook, J.W. 1932. The production of cancer by pure hydrocarbons-Part II. *Proc. Royal Soc. London S.B.* 11:485-496. (cited in IRIS).

Cottini, G.B. and G.B. Mazzone. 1939. The effects of 3,4-Benzpyrene on Human Skin. *Am J. Cancer.* 37: 186. (Cited in EPA, 1984e).

deSerres, F. and J. Ashby, Ed. 1981. Evaluation of Short-Term Tests for Carcinogens. *Reports on the International Collaborative Program.* Elsevier/North-Holland Biomedical Press, New York, p. 180, 190. (Cited in EPA, 1984e).

Deutsch-Wenzel, R., et al. 1983. Experimental studies in rat lungs on the carcinogenicity and dose-response relationships of eight frequently occurring environmental polycyclic aromatic hydrocarbons. *J. Nat'l. Cancer Inst.* 71 (3): 539-543. (cited in IRIS).

Fitzhugh. O.G. and W.H. Buschke. 1949. Production of Cataracts in rats by betatetralol and other derivatives of naphthalene. *Arch. Opthal.* 41: 572-583. (Cited in EPA 1984b).

Ghetti, C. and L. Mariani. 1985. Eye changes due to naphthalene. *Med. Lav.* 47: 524. (Cited in EPA, 1984b).

Hollstein, M. and J. McCann. 1979. Short-term tests for carcinogens and mutagens. Mutat. Res. 65: 133-226. (Cited in EPA, 1984e).

Huggins, C. and N.C. Yang. 1962. Induction and extinction of mammary cancer. Science 137 (3562): 257-262. (cited in IRIS).

IARC (International Agency for Research in Cancer). 1982. Chemicals, Industrial Processes and Industries Associated with Cancer in Humans, In: *IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans.* WHO, IARC, Lyon, France. Suppl. 4. (Cited in EPA, 1984e).

ICF, Clement Associates. 1985. *Chemical, Physical and Biological Properties of Compounds Present at Hazardous Waste Site.*

International Agency for Research on Cancer. 1983. *IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Human.*

Kaden, D.A., et al. 1979. Mutagenicity of Soot and Associated polycyclic aromatic hydrocarbons to Salmonella typhimurium. *Cancer Res.* 39:4152-4159. (cited in IRIS).

Kennaway, E.L. 1924. On cancer-producing tars and tar-fractions. *J. Ind-Hyg.* 5(12): 462-488. (cited in IRIS).

Klein, M. 1963. Susceptibility of strain B6AF/J Hybrid infant mice to tumorigenesis with 1,2-benzanthracene, deoxycholic acid, and 3-methyl-cholanthrene. *Cancer Res.* 23: 1701-1707. (cited in IRIS).

Knobloch K., S. Szendzikowski, and A. Slusarcyk - Zalobna. 1969. Acute and subacute toxicity of acenaphthene and acenaphthylene. *Med. Pracy.* 20(3): 210-222. CA 72(7) 299117b, (Cited in EPA, 1984f).

Mackenzie, K.M. and D.M. Angevine. Infertility in Mice Exposed *in utero* to Benzo(a)pyrene. *Biol. Reprod.* 24: 183-191. (Cited in EPA, 1983).

National Toxicology Program (NTP). 1980. Unpublished subchronic toxicity study: Naphthalene (C52904), Fischer 344 rats. Prepared by Battelle's Columbus Laboratories under subcontract no. 76-34-106002. (cited as principal RfD study in HEAST).

Neal, J. and R.H. Rigdon. 1967. Gastric Tumors in Mice Fed Benzo(a)pyrene: A quantitative Study. *Tex. Rep. Boil. Med.*, 25: 553. (Cited in EPA, 1984e).

Reshetyuk, A.L., E.I. Talakina, and P.a. En' yakova. 1970. Toxicological evaluation of acenaphthene and acenaphthylene. *Gig. Tr. Prof. Zabol.* 14(6): 46-47 CA 73(23)118650x, (Cited in EPA, 1984f).

Rigdon, R.H. and E.G. Rennels. 1964. Effect of Feeding Benzo(a)pyrene on Reproduction in the Rat. *Experientia.* 20: 224-226. (Cited in EPA, 1984e).

Rigdon, R.H. and J. Neal. 1969. Relationship of leukemia to lung and stomach tumors in mice feed benzo(a)pyrene. *Proc. Soc. Exp. Biol.* NY. 130: 146. (Cited in EPA, 1984e).

Robinson, J.R., J.S. Felton, R.C. Levitt, S.C. Thorgiersson, and D.W. Neber. 1975. Relationship Between "Aromatic Hydrocarbon Responsiveness" and the Survival Times in Mice Treated with Various Drugs and Environmental Compounds. *Mol. Pharmacal.* II: 850-865. (Cited in EPA, 1984e).

Schmahl, D. 1955. Examination of the carcinogenic action of naphthalene and anthracene in rats. *Z. Krebsforsch* 60:697-710. (cited in IRIS).

Sittig, M. 1991. *Handbook of Toxic and Hazardous Chemicals.*

Stanton, M.F., et al. 1972. Experimental induction of epidermoid carcinoma in the lungs of rats by cigarette smoke condensate. *J. Nat'l Cancer Inst.* 49(3): 867-877. (cited in IRIS).

Snell, K.C. and H.L. Stewart. 1962. Pulmonary adenomatose induced in DBA/2 mice by oral administration of dibenz (a,h) anthracene. *J. Natl Cancer Inst.* 28(5): 1043-1049. (cited in IRIS).

Snell, K.C., and H.L. Stewart. 1963. Induction of pulmonary adenomatose in DBA/2 mice by the oral administration of dibenz (a,h) anthracene. *Acta. Un. Int. Cancer* 19:692-694. (cited in IRIS).

Thyssen, J., J. Althoff, G. Kimmerle, and U. Mohr. 1981. Inhalation Studies with Benzo(a)Pyrene in Syrion Golden Hamsters. *J. Natl. Cancer Inst.* 66(3): 575-577. (Cited EPA, 1984e).

U.S. EPA. *Drinking Water Regulations and Health Advisories.*

U.S. EPA. 1984a. *Health Effects Assessment for Polycyclic Aromatic Hydrocarbons.* EPA 540/1-86/013.

U.S. EPA. 1984b. *Health Effects Assessment for Naphthalene.* EPA 600/8-89/094.

U.S. EPA. 1984c. *Health Effects Assessment for Phenanthrene.* EPA 540/1-86/029.

U.S. EPA. 1984d. *Health Effects Assessment for Pyrene.* EPA 540/1-86/030.

U.S. EPA. 1984e. *Health Effects Assessment for Benzo(a)pyrene.* Final Draft.

U.S. EPA. 1984f. *Health Effects Assessment for Acenaphthene.*

U.S. EPA. *Health Effects Assessment Summary Tables (HEAST).*

U.S. EPA. *Integrated Risk Information System* (IRIS).

U.S. EPA. 1986. *Superfund Public Health Evaluation Manual.*

U.S. EPA. 1988a. *Subchronic toxicity in mice with anthracene.* Final Report. Hazleton Laboratories, Ltd. Muskegon, MI. for the Office of Solid Waste, Wash, D.C. (cited in IRIS).

U.S. EPA. 1988b. *13-Week mouse oral subchronic toxicity study.* Toxicity Research Laboratories, Ltd. Muskegen, MI. for the office of Solid Waste, Wash, D.C. (cited in IRIS).

U.S. EPA. 1989d. *Mouse oral subchronic toxicity for Pyrene.* Study conducted by Toxicity Research Laboratories, Muskegon, MI. for the Office of Solid Waste, Wash., D.C. (cited in IRIS).

U.S. EPA, OERR. *CERCLA Compliance With Other Laws Manual Interim Final.* August, 1988.

U.S. EPA. 1986. *Quality Criteria for Water.* EPA 440/5-86-001.

U.S. EPA. 1989a. *Mouse oral subchronic study with acenaphthene.* Study conducted by Hazleton Laboratories, America, Inc. for the Office of Solid Waste, Wash., D.C. (cited in IRIS).

U.S. EPA. 1989b. *Subchronic toxicity in mice with anthracene.* Final Report Hazleton Laboratories, America, Inc. Prepared for the Office of Solid Waste, Wash. D.C. (cited in IRIS).

U.S. EPA. 1989c. *Mouse oral subchronic toxicity study.* Prepared by Toxicity Research Laboratories, Ltd. Muskegon, MI. for the Office of Solid Waste, Wash., D.C. (cited in IRIS).

Wislocki, P.G., et al., Tumorigenicity of nitrated derivatives of pyrene, benz(a)anthracene, chrysene, and benzo(a)pyrene in the newborn mouse assay. *Carcinogenesis.* 7(8):1317-1322. (cited in IRIS).

Wolf, O. 1976. Cancer Diseases in Chemical Workers in a Former Naphthalene Cleaning Plant. *Deutsche Gesundheituesen.* 31: 996. (Cited in EPA, 1984b)

Wynder, E.L. and D. Hoffman. 1959. A study of tobacco carcinogenic. VII. The role of higher polycyclic hydrocarbons. *Cancer* 12: 1079-1089. (cited in IRIS).

Van Duuren, B.L., et al. 1966. The tumor-promoting agents of tobacco leaf and tobacco

TABLE 1. CHEMICAL AND PHYSICAL PROPERTIES OF PAHs (U.S. EPA, 1986)

Compound	Chemical Formula	MW	SP. GR. (at 20°C)	BP (°C)	MP (°C)	VP (mmHg at 20°C)	Solubility (at 25°C)
Acenapthene	$C_{12}H_{10}$	154.21	1.225 at 0°C	279	96.2	$1.55x10^{-3}$	water: 3.42 mg/l organics: ethanol, toluene, chloroform, benzene
Acenaphthylene	$C_{12}H_8$	152.21			92.0*	$1x\ 10^{-3}$	water: 3.93 mg/1
Anthracene	$C_{14}H_{10}$	178.2	1.25	342	218	$1.95x10^{-4}$	water: 0.0446 mg/kg organics: benzene, chloroform, methanol
Benzo(a)anthracene	$C_{18}H_{12}$	228.30		435	167.0	2.2x10 at 20°C	water: 9.4 µg/kg organics: alcohol, ether, acetone, benzene,
Benzo(a)pyrene	$C_{20}H_{12}$	252.30		311	179.15	$5.6x10^{-9}$	water: 1.2 µg/kg organics: most
Benzo(b)fluoranthene	$C_{20}H_{12}$	252.3			168.3	$5.0x10^{-7}$	water: 0.014 mg/l organics: benzene, acetone
Benzo(k)fluoranthene	$C_{20}H_{12}$	252.3		480	215.7	$5.1x10^{-7}$	water: 0.0043 mg/l organics: acetic acid, benzene, ethanol
Benzo(g,h,i)perylene	$C_{22}H_{12}$	276.30			278.3	$1.03x10^{-10}$	water: 0.7 µg/kg organics: benzene, acetone
Dibenzo(a,h)anthracene	$C_{22}H_{14}$	278.4			266.6	$1.1x10^{-10}$	water: insoluble organics: benzene, toluene, xylene, oils

(Continued)

TABLE 1. (Continued)

Compound	Chemical Formula	MW	SP. GR. (at 20°C)	BP (°C)	MP (°C)	VP (mmHg at 20°C)	Solubility (at 25°C)
Chrysene	$C_{18}H12$	228.20	1.274	448	255.5	$6.3x10^{-9}$	water: 1.8 µg/kg organics: benzene, ether, alcohol
Fluoranthene	$C_{16}H_{10}$	202.24	1.252	250.5	111.1	$5.0x10^{-6}$	water: 0.206 mg/kg organics: acetic acid, benzene, chloroform, ethanol
Fluorene	$C_{13}H_{10}$	166.2		295	116.5	10 at 146°C	water: insoluble organics: most
Indeno(1,2,3-c,d)pyrene	$C_{22}H_{12}$	276.3			163.6	10^{-10} torr	water: insoluble organics:
2-Methylnapthalene	$C_{11}H_{10}$	142.20		241.05	34.58		water: insoluble organics: most
Naphthalene	$C_{10}H_8$	128.16	1.15	217.9	80.55	0.082	water: 31.7 mg/l organics:
Phenanthrene	$C_{14}H_{10}$	178.22	1.025	340.0	100	6.8x10	water: 1 mg/kg organics: ethanol, toluene, benzene
Pyrene	$C_{16}H_{10}$	202.24		385	149.5	$2.5x10^{-6}$	water: 0.132 mg/kg organics: benzene, diethyl ether, ethanol, toluene, acetone

TABLE 2. STANDARDS, CRITERIA AND GUIDELINES FOR PAHs(a)

Compound	EPA Carc. Class	Slope Factor Inh/Oral (mg/kg/day)$^{-1}$*	Chronic Oral RfD (mg/kg/day)	Chronic Inhalation RfD (mg/kg/day)	Subchronic Oral RfD(b) (mg/kg/day)	Subchronic Inhalation RfD (mg/kg/day)	MCL(c) (mg/l)	Ambient Water Quality Criteria (d) Fish & Water Consumption	Fish Consumption
	8							2.8 ng/l**	31.1 ng/l**
Acenapthene	--	--	$6.0x10^{-2}$	--	$6.0x10^{-1}$	--	--		
Acenapthylene	D	--	p	--	--	--	NA		
Anthracene	D	--	$3.0x10^{-1}$	--	$3.0x10^{0}$	--	NA		
Benzo(a)anthracene	B2	--/5.79 x 10^{-1}	--	--	--	--	0.0001		
Benzo(a)pyrene	B2	--/5.79 x 10^{0}	--	--	--	--	0.0002		
Benzo(b)fluroanthene	B2	--/5.79 x 10^{-1}	--	--	--	--	0.0002		
Benzo(k)fluroanthene	B2	--/5.79 x 10^{-1}	--	--	--	--	0.0002		
Benzo(g,h,i)perylene	D	ND/ND	--	--	--	--	NA		
Chrysene	B2	--/5.79 x 10^{-2}	--	--	--	--	0.0002		
Dibenz(a,h)anthracene	B2	--/5.79 x 10^{0}	--	--	--	--	0.0003		
Fluoranthene	D	--	$4.0x10^{-2}$	--	$4.0x10^{-1}$	--	--	42 µg/l	54 µg/l
Fluorene	D	--	$4.0x10^{-2}$	--	$4.0x10^{-1}$	--	NA		
Indeno(1,2,3-c,d)pyrene	B2	--/5.79 x 10^{-1}	--	--	--	--	0.0004		
2-Methylnapthalene	--	--	--	--	--	--	--		
Naphthalene	D	--	$4.0x10^{-3}$(b)	--	$4.0x10^{-2}$	--	NA		
Phenanthrene	D	--	--	--	--	--	NA		
Pyrene	D	--	$3.0x10^{-2}$	--	$3.0x10^{-1}$	--	NA		

*Values derived from B(a)P slope factor listed on IRIS by applying Toxic Equivalency Factors (TEFs).
-- = no data
NA = not available
ND = not determined
** = PAHs, in general (from U.S. EPA, Quality Criteria for Water, May 1986)
p = pending; currently under review by EPA.
References:
(a) U.S. EPA, Integrated Risk Information System (IRIS).
(b) U.S. EPA, Health Effects Assessment Summary Tables (HEAST).
(c) U.S. EPA, Drinking Water Regulations and Health Advisories.
(d) U.S. EPA, OERR, CERCLA Compliance With Other Laws Manual, Interim Final, August 1988.

POLYCHLORINATED BIPHENYLS

Background

The name polychlorinated biphenyl (PCB) categorizes any biphenyl ring in which one or more hydrogen is replaced by a chlorine atom. In commercial PCB mixtures, 40 to 70 different chlorinated biphenyl compounds can be present.

This profile is concerned with PCB-1260, -1254, and -1248, also known as Arochlors. Any statements made, unless otherwise specified, characterize these three PCBs.

Use

PCBs belong to a class of chemically stable, multi-use industrial chemicals that have been distributed widely in the ecosystem (EPA, 1985). PCBs were used in transformers and capacitors as dielectric insulating fluids because of their fire resistant qualities. In 1974, approximately 70 percent of domestically sold PCBs (34 million pounds) were used in capacitors while the remainder was used in transformers. An additional 450,000 pounds were imported for use in investment casting waxes, semi-enclosed heat transfer applications and mining equipment. The use of PCBs in capacitors began in 1930 and was discontinued in 1978. However, most of the electrical equipment containing PCBs are still in service (EPA, 1985).

Chemical and Physical Properties

Chemical Formula: $(C_6H_5Cl_x)_2$

MW: 189-399*
SG: 1.3 to 1.5 at 20°C*
FP: 300 - 500°F*
Sol. (water): 0.003 - 60.6 mg/l
Sol. (organics): soluble in most

BP: >267°C*
MP: 54-310°C
VP: 6.0×10^{-5} mmhg to 1.0×10^{-3} mmhg**

* increases with chlorination
**decreases with chlorination

Fate and Transport

PCBs are extremely persistent in soils containing moderate to high levels of organic matter. Heavily chlorinated PCBs persist longer and degrade slower than lightly chlorinated PCBs. PCBs are known to bioaccumulate readily in adipose tissues, especially in interstitial organisms.

In aquatic media, PCBs tend to volatilize, after which they may be slowly photolyzed in the atmosphere. Aquatic invertebrates are important in the cycling of PCBs within the aquatic environment and between aquatic and terrestrial ecosystems (Eisler, 1986).

Pharmacokinetics

Little data on PCB absorption are available. However, PCBs are expected to be absorbed almost completely in the gastrointestinal tract (90 percent for Aroclor 1248 at dose levels of 1.5 or 3.0 mg/kg body weight) (EPA, 1985). Studies in which PCBs are placed in the diet of Sprague-Dawley dams revealed that tissue concentrations vary in the following descending order: adipose tissue, mammary glands, kidney, liver, and lung. When Aroclor 1254 was administered at 0.25 to 50 mg/kg in the diet of rats starting on day 8 of gestation and continuing through postpartum day 14, the concentration of PCBs in milk was found to be 293 µg/ml by postpartum day 14 (EPA, 1985). Generally, it seems that the degree of chlorination greatly influences the rate of metabolism; the more heavily chlorinated the biphenyl moiety, the slower its metabolism (EPA, 1985). Data on the excretion of PCBs were not available, however, PCBs are expected to be eliminated via the urine (EPA, 1985).

Human Toxicity

Noncarcinogenic Effects

Systemic Effects

Exposure to PCB fumes results in acneform eruptions, irritation to the respiratory passages, and injury to the liver (ACGIH, 1984). These effects were noted at airborne PCB levels as low as 0.1 g/m^3 (EPA, 1985). Many studies of occupational exposure to PCBs have shown varying degrees of dermatologic and hepatic effects. Accidental human ingestion of PCB-contaminated rice oil in Japan in 1968 resulted in similar symptoms but also included headaches, vomiting, and spasms (ACGIH, 1984).

Teratogenic and Other Developmental Effects

Little evidence of teratogenicity was found in the scientific literature reviewed; most reports concentrated on the fetotoxicity of PCBs. Infants of monkeys exposed to 2.5 ppm Aroclor 1248 in the diet for 6 months before mating were born with hyperpigmentation (EPA, 1984). Reduced birth weights were observed in infants from monkey exposed to 1.0 ppm Aroclor 1016 in the diet. Nursing resulted in the loss of facial hair, edema of the eyelids, gastric hyperplasia, vomiting, liver degeneration, and other signs of PCB-induced toxicity, (EPA, 1984). Dams, exposed to PCB concentrations of 8 mg/kg/day orally, showed sign of lethargy and vaginal bleeding (EPA, 1984).

In one study, Aroclor 1254 was given orally to rabbits at doses of 1, 10, 12.5, 25.0, 50.0 mg/kg-bw for the first 28 days of gestation. At a dose level of 12.5

mg/kg-bw/day, adverse reproductive effects were observed (resorptions, aborted fetuses, decreased litter size). Aroclor 1248 at 2.5 or 5 ppm (0.06 or 0.12 mg/kg/day) in the diet for up to 6 months has been demonstrated to prolong the menstrual cycle in Rhesus monkeys (EPA, 1985).

Mutagenic Effects

The mutagenic activity of PCB mixtures and isomers was studied using *Salmonella typhimurium* (TA1538) in the presence of a microsomal activation system. Aroclor 1221 and 4-chlorobiphenyl were significantly mutagenic in the assay system (EPA, 1985).

Carcinogenic Effects

PCBs are considered Class B2 carcinogens, probable human carcinogens. Human studies are not adequate. In a number of studies on the effects of occupational exposure to PCB fumes, statistically significant evidence points toward carcinogenicity, but these studies did not note the presence or absence of other carcinogens. In the aforementioned studies, polychlorinated dibenzofurans and quinones were also present in the PCB-contaminated rice oils (IRIS).

Norback and Weltmann (1985) fed 140 Sprague-Dawley rats a diet of corn oil mixed with Aroclor 1260 at 100 ppm for 16 months. They followed that with a diet containing 50 ppm Aroclor for 8 months and then a basal diet for 5 months. Female rats exhibited a 91 percent incidence of hepatocellular carcinoma. Males exhibited a 4 percent incidence of carcinoma and an 11 percent incidence of neoplastic nodules.

Other studies on laboratory animals indicated an increase in carcinogenesis amongst PCB exposed animals. From most studies, it appears as though exposure to the more heavily chlorinated PCBs results in an increased risk of cancer.

Ecotoxicity

Polychorinated biphenyls are bioaccumulated and can be biomagnified, therefore, their toxicity increases with length of exposure and position of the exposed species on the food chain (ICF, 1985). Chronic exposure of PCBs for rainbow trout, bluegills, and channel catfish yielded LC_{50} values of about 0.1 mg/liter. Invertebrate species are also adversely affected, with some species having 7-day LC_{50} values as low as 1 µg/liter (ICF, 1985). Present data imply that, in general, juvenile organisms appear more susceptible to the effects of PCBs than either eggs or adults (ICF, 1985), and lower chlorinated biphenyls are more toxic to aquatic organisms than higher chlorinated biphenyls (Eisler, 1986). It is clear that based on the chronic values available in the literature, PCBs are highly toxic to both freshwater and saltwater aquatic life.

Diet is an important exposure route for PCB accumulation within terrestrial species. Sensitive bird species are susceptible to PCB poisoning, mainly as a result of eating contaminated fish

or bivalves. LD_{50}s for several avian species ranged from 604 to greater than 6,000 mg Arochlor/kg diet although reproductive impairment has been observed at 5 mg Arochlor/kg diet concentrations (Eisler, 1986). Documentation of PCB exposure to terrestrial animals is limited, however, mammals are generally more sensitive to acute PCB toxicity than birds. Mink are particularly sensitive as 0.64 mg/kg in their diet caused reproductive failure and LD_{50} concentrations less than 10 mg Arochlor/kg have been reported (Eisler, 1986).

Standards, Criteria and Guidelines

EPA Class B2 carcinogen

Oral Slope Factor:	7.7×10^{0} $(mg/kg/day)^{-1}$
Inhalation Slope Factor:	NA
Chronic Oral RfD:	NA
Chronic Inhalation RfD:	NA
Subchronic Oral RfD:	NA
MCL:	0.5 µg/L
AWQC:	Freshwater Acute - 2.0 µg/L
	Freshwater Chronic - 1.4×10^{-2} µg/L

BIBLIOGRAPHY

American Conference of Governmental Industrial Hygienists, *Documentation of Threshold Limit Values*, 1984.

Eisler, R. 1986. *Polychlorinated Biphenyl Hazards to Fish, Wildlife, and Invertebrates: a Synoptic Review*. U.S. Fish and Wildl. Serv. Biol. Rep. 85 (1.7) 72 pp.

ICF Clement, *Chemical, Physical and Biological Properties of Compounds Present at Hazardous Waste Sites*, 1985.

Norback, D.H. and R.H. Weltman, Polychlorinated Biphenyl Induction of Hepatocellular Carcinoma in the Sprague-Dawley Rate, 1985, *Environ. Health Perspect.*, 60: 97-105, (Cited in IRIS).

Sittig, Marshall, *Handbook of Toxic and Hazardous Chemicals*, 1991.

U.S. EPA, *Drinking Water Regulations and Health Advisories.*

U.S. EPA, *Integrated Risk Information System (IRIS).*

U.S. EPA, OERR. *CERCLA Compliance With Other Laws Manual Interim Final.* August, 1988.

U.S. EPA, Research and Development, *Health Effects Assessment for PCBs*, EPA 540/1-86/004, 1984.

U.S. EPA, Office of Drinking Water, *Health Advisory for PCBs*, 1985.

INORGANICS

ALUMINUM

Use

Aluminum is used in the shipbuilding, electrical, aircraft, automobile, light engineering, and jewelry industries. Powdered aluminum is used in paints and the pyrotechnic industry.

Chemical and Physical Properties

Chemical Formula: Al

SG: 2.708
BP: 2450°C
MP: 660°C
Sol. (water): insoluble, soluble in acids and alkalies

Fate and Transport

Aluminum does not exist in the environment in its elemental form. It is, however, a constituent of many minerals. When exposed to air it becomes coated with aluminum oxide, which prevents further corrosion (EPA, 1980). Aluminum is generally not regarded as a water pollution problem (EPA, 1977).

Pharmacokinetics

Little information on aluminum pharmacokinetics was available.

Aluminum has been found in all human organs. The lungs, however, show a higher concentration than all other organs. This probably results from inhalation of dust or fumes (EPA, 1977). The presence of aluminum in human organs also indicates absorption through ingestion (Sittig, 1991). Ingestion of aluminum affects its concentration in the liver, brain, testes and blood (Ondreicka, et al., 1966). Various diseases also influence aluminum concentration of body organs (Sorensen et al., 1974).

Human Toxicity

Noncarcinogenic

Systemic Effects

Fibrotic lung disease and severe and fatal lung damage have been observed in workers exposed to dust of aluminum metal (EPA, 1977). Aluminum is suspected of inducing neurotoxic effects, characterized by gradual loss of motor, speech, and cognitive functions. Another target organ for aluminum toxicity is the bone. Low bone formation or osteomalacia has been linked to aluminum exposure. A form of anemia, which is not related to iron deficiency,

has also been linked to aluminum exposure (EPA, 1992). Aluminum particles deposited in the eye may cause necrosis of the cornea (Sittig, 1991).

Teratogenic and Developmental Effects

Muller et al. (1990) administered 400 mg Al/kg/day to pregnant rats on days 1-7, 1-14 or 1-21 of gestation. No effects on maternal body weight or food intake were observed in dams on gestational days 1-7 or 1-14. In dams exposed on gestational days 1-21, a significant decrease in maternal body weight was observed. Aluminum tends to accumulate in the testes (EPA, 1980).

Mutagenic Effects

No information was available in the literature.

Carcinogenic Effects

Metallic aluminum was tested for carcinogenic activity, with no tumors resulting (Furst, 1971). EPA (1977) reported that carcinogenicity studies have failed to produce cancer in experimental animals. Other studies (Milham, 1979p; Anderson et al., 1982) indicate, however, a possible cancer risk from aluminum exposure.

No definite conclusion regarding the carcinogenicity of aluminum can be made from the available literature.

Ecotoxicity

Aluminum concentrations in water of over 1.5 ppm causes physiological and behavioral changes in rainbow trout (Freeman and Everhart, 1971). Aluminum seems to be toxic to plants at soil pH values below five (EPA, 1980).

Standards, Criteria and Guidelines

EPA Class D Carcinogen

Oral Slope Factor: NA
Chronic Oral RfD: 1×10^0 mg/kg/day
Subchronic Oral RfD: 1×10^0 mg/kg/day
MCL: NA
AWQC: Acute: 750 µg/L
Chronic: 87 µg/L
(pH dependent)

BIBLIOGRAPHY

Anderson, H., B.E. Dahlberg, K. Magnus and A. Wannag. 1982. Risk of cancer in the Norwegian aluminum industry. *Int. J. Cancer.* 29:295-298 (cited in U.S. EPA, 1992).

Freeman, R.A., and W.H. Everhart. 1971. Toxicity of aluminum hydroxide complexes in neutral and basic media to rainbow trout. *Trans. Am. Fish Soc.* 100(4):644-658 (cited in U.S. EPA, 1980).

Furst, A. 1971. Trace elements related to specific chronic diseases: Cancer. *Geol. Soc. Am. Memoir.* 21:475-480 (cited in U.S. EPA, 1992).

Milham. S. 1979. Mortality in aluminum reduction plant workers. *J. Occupat. Med.* 21:475-480 (cited in U.S. EPA, 1992).

Muller, G., V. Bernuzzi, D. Desor, M-F. Hutin, D. Burnel, and P.R. Lehr. 1990. Developmental alterations in offspring of female rats orally intoxicated by aluminum lactate at different gestation periods. *Teratol.* 38:253-261 (cited in U.S. EPA, 1992).

Ondreika, R. Ginter, E. and Kortus, J. 1966. *Brit. J. Ind. Med.* 23, 305-312 (cited in Toxicology of Metals - Volume II).

Sittig, Marshal. 1991. Handbook of Toxic and Hazardous Chemicals and Carcinogens.

Sorensen, J.R.J., Campbell, I.R., Tepper, L.B. and Ling, R.D. 1974. *Environ. Health Perspect.* 7, 3-95 (cited in Toxicology of Metals - Volume II).

U.S. EPA. 1977. Toxicology of Metals - Volume II. EPA-600/1-77-022.

U.S. EPA. 1980. Chemical Hazard Information Profiles. EPA-560/11-80-011.

U.S. EPA. 1992. Memorandum from J. Dollarhide, Chemical Mixtures Assessment Branch to M. Walters, U.S. EPA Region II, on the toxicity and carcinogenicity of aluminum.

ANTIMONY

Use

Antimony is widely used as an alloy constituent in pewter and white metal, and is used in the manufacture of storage battery plates, solder, and ammunition because of its strength and its resistance to corrosion (Sittig, 1991). It is used as a fire-retardant in textiles and is used to dye steel, aluminum, pewter, and zinc (Sittig, 1991). One compound, antimony potassium tartrate, is used in medicine and as a leather mordant (ACGIH, 1984).

Chemical and Physical Properties

AG: 121.75 BP: 1750°C
SG: 6.684 at 25°C MP: 630.74°C
Sol.(water): Insoluble
Sol.(organics): Insoluble

Fate and Transport

Antimony is present naturally in water bodies as antimony oxide. Antimony oxide is generally reduced to stibine (SbH_3) in benthic sediments. Stibine is highly volatile and is very soluble in water but, in aerobic environments, it is rapidly oxidized to Sb_2O_3. In anaerobic waters, antimony compounds are quite soluble and, when present in rivers and lakes, they rapidly transport to oceans (ICF, 1985). Antimony is known to sorb to clays and minerals so, in soils, antimony would be expected to remain stable. Particulate antimony compounds are known to transport well in the atmosphere (ICF, 1985).

Pharmacokinetics

No pertinent information was located regarding the pharmacokinetics of antimony. It appears as though antimony primarily effects the lungs upon inhalation. Ingestion of antimony leads to kidney and liver damage (ACGIH, 1984) suggesting absorption occurs in these organs.

Human Toxicity

Noncarcinogenic

Systemic Effects

Schroeder et al. (1970) reported that rats administered 5 ppm potassium antimony tartrate in water exhibited reduced lifespans and altered blood chemistries; no increased incidence in tumors was seen.

One study reported that, of 125 workers employed in the abrasives industry, 6 died suddenly and two died of chronic heart disease. Upon examination of 75 of the workers, 37 exhibited EKG problems, 14 had high blood pressure, and 7

had ulcers (ACGIH, 1984). Ambient air levels were found to range from 3 to 5 mg/m^3. These problems were confirmed to be a result of antimony exposure when rats, rabbits, and dogs were exposed to similar concentrations in the air (3.7 to 5.6 mg/m^3). Cardiac dysfunction and parenchymatous degeneration of the myocardium were noted in all species. Chronic inhalation of antimony trioxide caused severe pneumonitis in guinea pigs (ACGIH, 1984).

Teratogenic and Other Developmental Effects

Human case studies suggest that antimony may cause an increase in spontaneous abortions and several other gynecological disorders (ICF, 1985). Decreased weight gain was observed in babies born to mothers exposed to antimony compounds (ICF, 1985).

Mutagenic Effects

Several bacterial studies indicate that antimony compounds are mutagenic (ICF, 1985).

Carcinogenic Effects

Antimony has been shown to increase lung cancer among exposed workers. An inhalation study performed on rats indicated that antimony trioxide increases the risk of lung and liver tumors (ICF, 1985). The number of studies performed, however, has been inadequate to categorize antimony as a carcinogen. EPA has not evaluated antimony for evidence of human carcinogenic potential.

Ecotoxicity

LC_{50} values for the freshwater species, *Daphnia magna,* and the fathead minnow, range between 9,000 and 21,900 mg/l. No detectable bioconcentration of antimony was noted in bluegill (ICF, 1985).

No data regarding toxicity of antimony to terrestrial species other than laboratory species were located in the available literature.

Standards, Criteria and Guidelines

Unclassified by EPA as to carcinogenicity

Oral Slope Factor: NA
Chronic Oral RfD: 4.0×10^{-4} mg/kg/day
Subchronic Oral RfD: 4.0×10^{-4} mg/kg/day
MCL: 0.006 mg/L
AWQC: Acute: 88 µg/L (proposed)
Chronic: 30 µg/L (proposed)

BIBLIOGRAPHY

American Conference of Governmental Industrial Hygienists. 1984. *Documentation of the Threshold Limit Values.*

ICF Clement. 1985. *Chemical, Physical, and Biological Properties of Compounds Present at Hazardous Waste Sites.*

Schroeder, H.A., M. Mitchner, and A.P. Nasor. 1970. Zirconium, Niobium, Antimony, Vanadium, and Lead in Rats: Life Term Studies. *J. Nutr.* 1000:59-66. (Cited in IRIS).

Sittig, M. 1991. *Handbook of Toxic and Hazardous Chemicals.*

U.S. EPA. *Drinking Water Regulations and Health Advisories.*

U.S. EPA. *Health Effects Assessment Summary Tables (HEAST).*

U.S. EPA. *Integrated Risk Information System (IRIS).*

U.S. EPA, OERR. *CERCLA Compliance With Other Laws Manual Interim Final.* August, 1988.

U.S. EPA. 1986. *Quality Criteria for Water* EPA 440/5-86-001.

ARSENIC

Use

Arsenic can be found in the environment in four valence states (-3, 0, +3, +5) and is used industrially in the form of arsenic disulfide, arsenic pentoxide, arsenic trichloride, arsenic trisulfide and lead arsenate, but primarily as arsenic trioxide. Elemental arsenic is a shiny, gray element that possesses both metallic and non-metallic properties. It is present naturally in the environment at low concentrations and is used industrially as arsenic trioxide, in pigment production, glass manufacturing, textile printing, tanning, and in antifouling paints. As arsenic trichloride, it is used in the manufacture of pharmaceuticals (Sittig, 1991).

Metallic arsenic is used as an alloying agent in the smelting of copper, zinc and lead ores.

Chemical and Physical Properties

AW: 74.91 BP: 613°C
SG: 5.72 at 20°C MP: 817°C
VP: 1 mmhg at 372°C
Sol. (water): insoluble (except for some salts).

Fate and Transport

Arsenic is generally quite mobile in the environment although, because it occurs in four valence states, it cannot be characterized easily. The most common fate processes of arsenic in the environment are speciation between the +3 and +5 valence states, volatilization, sorption, and biotransformation (EPA, 1984).

In surface waters, arsenic is significantly influenced by the presence of biota. Arsenic is readily bioaccumulated but is often biotransformed to methylated arsenicals, volatile compounds that evaporate from surface waters (EPA, 1985).

In surface soils, arsenic is known to sorb to clays, iron oxides, and particulate matter. The presence of these materials would greatly retard arsenic's leachability (EPA, 1984). In soils with low sorptive capacity, arsenic will leach into ground water, where it would likely be transported readily.

The primary means of removal of atmospheric arsenic are wet and dry precipitation (EPA, 1984).

Pharmacokinetics

Soluble arsenic salts are known to be easily absorbed through the gastrointestinal lining in humans and animals (Coulson, et al., 1935). In humans, peak blood arsenic levels (98 percent of total arsenic ingested) were reached after only 24 hours following the ingestion of 8.25 mg As in three doses (EPA, 1985). Arsenic is distributed, in humans, primarily to the

nails, hair, bone and skin, and to a lesser extent, the heart, liver, kidneys and lungs (Kadowski, 1960).

In laboratory animals, arsenic was shown to distribute to the liver, kidneys, lung, spleen, skin, and brain. It is removed rapidly from all organs except for the latter two (EPA, 1985).

Arsenic generally is metabolized to methylated arsenicals such as monomethyl and dimethyl arsenic. Buchet, et al. (1981) reported that 25 percent of arsenic, administered as arsenate to human volunteers, was excreted in the urine as inorganic arsenic, 25 percent as monomethyl and 50 percent as dimethyl arsenic.

Lanz, et al. (1950) noted that, in contrast to a humans metabolic processes, rats retain arsenic in their red blood cells for as long as 180 days. Humans typically remove 90 percent of ingested arsenic within 4 days.

Human Toxicity

Noncarcinogenic Effects

Systemic Effects

Arsenic is known to be highly toxic to humans. Subchronic exposure of infants to 3 mg/day arsenic in contaminated milk caused several deaths, according to Hamamoto (1955). Oral exposure to 50 to 300 mg of inorganic arsenic was the probable cause of death to several workers, according to Vallee, et al. (1960). From these two case studies, a subacute lethal dose of 0.6 mg/kg/day was estimated for humans (ATSDR, 1989).

Oral exposure of humans to arsenic is known to cause nausea, vomiting, diarrhea, and other gastrointestinal disorders (ATSDR, 1989). Long-term exposure results in paresthesia, weakness, anorexia, bronchitis, and various skin disorders (EPA, 1985). It was reported that children exposed to 0.8 mg/L arsenic in drinking water exhibited evidence of myocardial infarction and arterial thickening (ATSDR, 1989). In Taiwan, chronic exposure to arsenic in drinking water was thought to cause gangrene in the feet and toes in 0.9 percent of the population ("Blackfoot disease"). Concentrations were reported to average 0.5 mg/L arsenic (Tseng, 1977; Tseng et al., 1968).

Exposure to arsenic doses ranging from 2.8 to 5.7 mg/kg/day in newborn Rhesus monkeys caused death in 75 percent of monkeys in the 5.7 mg/kg/day group and death in two of the seven monkeys in the 2.8 mg/kg/day group. Death was attributed to hemorrhaging, edema, and necroses of the brain (EPA, 1985). All of the surviving monkeys had normal cardiovascular and neurological function.

Teratogenic and Other Developmental Effects

Parenteral administration of 10 to 45 mg/kg/day of sodium arsenate to pregnant rats, mice, and hamsters has been reported to increase the frequency of fetal malformations (ATSDR, 1989). Arsenic has also been shown to be teratogenic when administered orally. Hood, et al. (1977) found that a single gavage dose of 29 mgAs^{+5}/kg administered to pregnant mice on day 9, 10 or 11 of gestation resulted in death or resorption of 17-26 percent of the fetuses. Of the live fetuses, 10-16 percent were below average in weight and 1-3 percent were severely malformed.

Mutagenic Effects

Arsenic is known to cause DNA fragmentation and sister chromatid exchange in several cell types in laboratory animals and humans (ATSDR, 1989).

Carcinogenic Effects

Arsenic is classified by EPA as a Class A carcinogen, a known human carcinogen. Oral exposure to elevated levels of arsenic unequivocally increases the risk of skin cancer. Tseng, et al. (1968) and other researchers noted a significant increase in several skin cancer types in populations exposed to elevated arsenic levels in the drinking water (ATSDR, 1989).

Numerous studies of smelter workers have indicated that occupational exposure to arsenic is directly associated with lung cancer (IRIS, 1990). Matanoski, et al. (1981) reported that residents surrounding a pesticide manufacturing plant were at a greater risk of contracting lung cancer than the normal population.

In a supplemental paper, Tseng reported a significant increase in the incidence of bladder, lung, kidney, and colon cancer in a Taiwanese population exposed to elevated arsenic levels in their drinking water.

All evidence from human case studies indicates that chronic exposure to arsenic causes cancer. In laboratory studies, however, attempts to induce cancer in animals have been inconclusive or negative (ATSDR, 1989). Some studies, in which the arsenic retention time has been artificially increased, have shown that arsenic will produce tumors in rats (ATSDR, 1989).

Ecotoxicity

Arsenic compounds are acutely toxic to both freshwater and saltwater species of organisms, with early life stages being the most susceptible (ICF, 1985). Toxicity can occur at levels as low as 19 µg/l in sensitive aquatic species. Saltwater fish species are susceptible to arsenic's toxic effects at levels around 15 mg/l, but some invertebrates are affected at around 508 µg/l

(ICF, 1985). Although arsenic may be bioaccumulated by aquatic organisms, arsenic is not biomagnified in the food chain (Eisler, 1988).

Arsenic poisoning is generally attributed to an acute or subacute exposure period; chronic arsenic poisoning is seldom encountered in species other than man (Eisler, 1988). LD_{50} values (single oral doses) range from 17 to 48 mg/kg BW in birds and from 2.5 to 33 mg/kg BW in mammals (Eisler, 1988).

Standards, Criteria and Guidelines

EPA Class A Carcinogen

Oral Slope Factor:	1.75×10^{0} $(mg/kg/day)^{-1}$
Chronic Oral RfD:	3.0×10^{-4} mg/kg/day
Subchronic Oral RfD:	3.0×10^{-4} mg/kg/day
MCL:	0.05 mg/L
AWQC:	Acute: 360 µg/L
	Chronic: 190 µg/L
	(Trivalent State)

BIBLIOGRAPHY

American Conference of Governmental Industrial Hygienists. 1984. *Documentation of the Threshold Limit Values.*

Agency for Toxic Substance and Disease Registry (ATSDR). 1989. *Toxicity Profile for Arsenic.*

Buchet, J.P., R. Lauwerys, and H. Roels. 1981. Comparison of the Urinary Excretion of Arsenic Metabolites After a Single Oral Dose of Sodium Arsenite, Monoethyl Arsonate or Dimethyl Arsenate in Man. *Int. Arch. Occup. Environ. Health.* 48:71-79. (Cited in EPA, 1985).

Coulson, E.J., et al. 1935. Metabolism in the Rat of the Nautrally Occurring Arsenic of Shrimp as Compared with Arsenic Trioxide. *J. Natr.* 10:255. (Cited in EPA, 1985).

Hood, R.D., G.T. Thacker, and B.L. Patterson. 1977. Effects in the Mouse and Rat of Prenatal Exposure to Arsenic. *Environ. Health Perspect.* 19:219-222. (Cited in EPA, 1985).

Eisler, R. 1988. Arsenic hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish Wildl. Serv. Biol. Rep. 85 (1.12). 92 pp.

Enterline, P.E. and G.M. Marsh. 1982. Cancer among workers exposed to arsenic and other substances in a copper smelter. *Am. J. Epidemio.* 116:895-911. (cited in HEAST).

ICF, Clement Associates. 1985. *Chemical, Physical and Biological Properties of Compounds Present at Hazardous Waste Sites.*

Kadowski, K. 1960. Studies on the Arsenic Contents of Organ Tissues of the Normal Japanese. *Osaka Med. Jour.* 9:2083. (Cited in EPA, 1985).

Lanz, H. Jr., et al. 1950. The Metabolism of Arsenic in Laboratory Animals Using AS^{74} as a Tracer. *Univ. Calif. Publ. Pharmacal.* 2:263. (Cited in EPA, 1985).

Matanoski, G.E. Landau, J. Tonascia, C. Lazar, E. Elliot, W McEnroe, and K. King. 1981. Cancer Mortality in an Industrial Area of Baltimore. *Environ. Res.* 25:2-8. (Cited in IRIS)

Sittig, M. 1991. *Handbook of Toxic and Hazardous Chemicals.*

Tseng, W.P., et al. 1968. Prevalence of Skin Cancer in an Endemic Are of Chronic Arsenicism in Taiwan. *J. Natl. Cancer Inst.* 40:453-463. (Cited in IRIS).

Tseng, W.P. 1977. Effects and dose-response relationships of skin cancer and blackfoot disease with arsenic. *Environ. Health Perspec.* 19:109-119. (cited in IRIS).

U.S. EPA. *Drinking Water Regulations and Health Advisories.*

U.S. EPA. 1985. Office of Drinking Water. *Health Advisory for Arsenic.*

U.S. EPA. 1985. *Health Effects Assessment for Arsenic.*

U.S. EPA. *Integrated Risk Information System (IRIS).*

U.S. EPA. *Health Effects Assessment Summary Tables (HEAST).*

U.S. EPA, OERR. *CERCLA Compliance With Other Laws Manual Interim Final.* August, 1988.

U.S. EPA. 1986. *Quality Criteria for Water.* EPA 440/5-86-001.

BARIUM

Use

Barium, a silver white metal, is produced by reduction of barium oxide. In its metallic state, it is used for the removal of residual gas in vacuum tubes and in alloys with nickel, lead, calcium, magnesium, sodium, and lithium.

Barium compounds are used in the manufacture of a variety of products including lithopone (a white pigment in paints), chlorine, sodium hydroxide, valves, and green flares. They are used in synthetic rubber vulcanization, x-ray diagnostic work, glassmaking, papermaking, beet-sugar purification, and animal and vegetable oil refining. They can be found in use in the brick and tile, pyrotechnics, and electronics industries. These compounds are found in lubricants, pesticides, glazes, textile dyes and finishes, pharmaceuticals, and in saltwater cements. Barium is used as a rodenticide, a flux for magnesium alloys, a stabilizer and mold lubricant in the rubber and plastics industries, an extender in paints, a loader for paper, soap, rubber, and linoleum. It is used as a fire extinguisher for uranium and plutonium fires as well (Sittig, 1991).

Chemical and Physical Properties

AW: 137.3 MP: 725°C
SG.: 3.5 BP: 1640°C
Sol. (water): decomposes, combines with sulfate present in natural waters to form $BaSO_4$, which has a solubility of 1.6 mg/l at 20°C.
Sol. (organics): alcohol, insoluble in benzene.

Fate and Transport

Being extremely reactive, barium decomposes in water, and readily forms insoluble carbonate and sulfate salts. In surface or ground waters it is generally found in solution only in trace amounts. Large amounts will not dissolve because of the sulfate found in most natural water (barium sulfate has a low solubility). In water that contains more than a few ppm sulfate, barium will not dissolve at more than a few ppm. Barium sulfate may become considerably more soluble in the presence of chloride and other anions.

It is rare to find barium in drinking water at concentrations greater than 1 mg/l. Atmospheric transport of barium, in the form of particulates, can occur. Bioaccumulation is insignificant for barium (ICF, 1985).

Because of its formation of water-insoluble salts and its inability to form soluble complexes with humic and fulvic materials, barium is not expected to be very mobile in soils. However, some water insoluble barium compounds may be solubilized under acidic conditions and thereby move back into groundwater (US EPA, 1984).

Pharmacokinetics

Barium and its compounds can affect the heart, lungs, central nervous system, skin, respiratory system, and eyes (Sittig, 1991).

Although quantitative data for the absorption of barium from the GI tract was not found in the literature reviewed, McCauley and Washington (1983) found relative absorption rates for barium salts with barium chloride having greater absorption than barium sulfate which, in turn, had greater absorption than barium carbonate.

Gore and Patrick (1982) reported that barium sulfate administered intratracheally to rats was concentrated in the area immediately beneath the basement membrane within 24 hrs. and remained in this area for at least 7 days. This suggests a degree of absorption from the respiratory tract.

Human Toxicity

Noncarcinogenic Effects

Systemic Effects

Wones et al. (1990) administered barium (as barium chloride) in the drinking water of eleven healthy male volunteers. Subjects ranged in age from 27-61 years and had no previous history of diabetes, hypertension, or cardiovascular disease. Diets were strictly controlled throughout the 10-week study. Subjects were given 1.5 l/day of distilled, charcoal-filtered water with 0 mg/l barium for weeks 0-2, 5 mg/l for weeks 3-6, and 10 mg/l for weeks 7-10.

No changes in blood pressures or serum chemistry were detected. An increase in serum calcium levels, attributed to a decrease in serum albumin levels, although statistically significant, was not clinically significant. An NOAEL of 0.21 mg/kg/day was identified in this study.

Brenniman and Levy (1984) conducted a retrospective epidemiological study by comparing human mortality and morbidity rates in populations ingesting elevated barium levels (2-10 mg/l) in their drinking water to populations ingesting little or no barium (less than or equal to 0.2 mg/l). Differences in mortality rates from cardiovascular diseases were significantly higher in the communities with elevated barium. However, these differences were largely in the 65 and over age group and did not take population mobility, the use of water softeners, or medications into account. Differences in blood pressure, prevalence of hypertension, stroke, and heart and renal disease were also measured and no significant differences occurred between the populations.

In a variety of animal studies (McCauley, 1985; Perry et al., 1983; Schroeder and Mitchener, 1975a,b; Tardiff et al., 1980) no signs of barium toxicity were

found at any dose level. Animals treated with the highest dose of barium, 1000 mg/l in McCauley's study did exhibit ultrastructural changes in the kidney glomeruli and the presence of myelin figures (IRIS).

Taransenko et al. (1977) reported on the effects barium carbonate dust had on rats when inhaled. Male rats were exposed to the dust at levels of 5.2 and 1.15 mg/m^3, 4 hrs/day for 6 months. While the rats in the high dose group experienced what Taransenko called "general toxic effects" (decreased body weight, changes in hematologic parameters), the low dose animals exhibited no toxic effects.

Workers exposed to barium dust have been shown by occupational studies to develop "baritosis." No symptoms are illustrated other than a significantly higher incidence of hypertension (IRIS).

Teratogenic and Other Developmental Effects

Taransenko et al. (1977) reported that male rats exposed to an atmospheric concentration of 22.6 mg $BaCO_3/m^3$ for one cycle of spermatogenesis exhibited decrease number of spermatozoids and a lower percentage of motile sperm forms. Female rats exhibited increased mortality in subsequent litters and a general underdevelopment of newborn pups when exposed to 13.4 mg $BaCO_3/m^3$ for 4 months. An atmospheric concentration of 3.1 mg $BaCO_3/m^3$ produced no systematic effects, although some ovarian follicle atresia was observed. When males exposed to an atmospheric concentration of 5.2 mg $BaCO_3/m^3$, 4 hours/day for 4 months when mated with unexposed females, increased mortality of the fetuses resulted.

Mutagenic Effects

Nishioka (1975) found that repair deficient strains of *Bacillus subtillis* did not exhibit an increased mutation frequency when exposed to barium chloride. Loeb et al. (1978) obtained negative results as well in tests of the induction of errors in viral DNA transcription in vitro.

Carcinogenic Effects

Barium has not been evaluated by the US EPA for evidence of human carcinogenic potential (IRIS).

McCauley et al. (1985) found no carcinogenic effect in a study of the histological and cardiovascular effects of drinking water containing 0,10,100, and 250 mg/l barium for 16,36, and 68 weeks on male Sprague-Dawley rats. Female (rats???) were exposed to 0 or 250 mg/l barium for 46 weeks.

Schroeder and Mitchener (1976a,b) investigated the carcinogenicity of barium acetate in drinking water to both rats and mice. The observed differences in tumor incidence in the rats was insignificant statistically and there was essentially no difference in tumor incidence in the mice.

Ecotoxicity

There is sufficient sulfate or carbonate present in most natural water to precipitate any barium present in the water as a virtually insoluble, non-toxic compound. Therefore, it would require a soluble barium concentration of at least 50 mg/l before toxicity to both fresh and marine aquatic life would be expected (US EPA, 1986).

Standards, Criteria, and Guidelines

Unclassified by EPA as to carcinogenicity

Oral Slope Factor:	NA
Chronic Oral RfD:	7.0×10^{-2} mg/kg/day
Subchronic Oral RfD:	7.0×10^{-2} mg/kg/day
MCL:	2.0 mg/L

BIBLIOGRAPHY

Brenniman, G.R. and P.S. Levy. 1984. High Barium Levels in Public Drinking Water and Its Association with Elevated Blood Pressure. Advance in Modern Toxicology IX, E.J. Calabrese, Ed. Princeton Scientific Publications, Princeton, NJ. p. 231-249. (Cited in IRIS).

Gore, D.J. and G. Patrick. 1982. A Quantitative Study of the Penetration of Insoluble Particles into the Tissue of the Conducting Airways. *Ann. Occup. Hyg.* 26(1-4):149-161 (CA98:30673n). (Cited in HEA, 1984).

ICF, Clement Associates. 1985. *Chemical, Physical, and Biological Properties of Compounds Present at Hazardous Waste Sites.*

Loeb, L., et al. 1978. Infidelity of DNA Synthesis as Related to Mutagenesis and Carcinogenesis. *Adv. Exp. Med. Biol.* 91:209-217. (Cited in HEA, 1984).

McCauley, P.T., et al. 1985. Investigations into the Effect of Drinking Water Barium on Rats. *Environ. Health Perspect. Vol. IX,* E.J. Calabrese, Ed. Princeton Scientific Publications, Princeton, NJ. p. 197-210. (Cited in IRIS).

McCauley, P.T. and I.S. Washington. 1983. Barium Bioavailability as the Chloride Sulfate or Carbonate Salt in the Rat. *Drug. Chem. Toxicol.* 6(2):209-217 (CA99:17715d). (Cited in HEA, 1984).

Nishioka, H. 1975. Mutagenic Activities of Metal Compounds in Bacteria. *Mutat. Res.* 31:185-189. (Cited in HEA, 1984).

Perry, H.M., et al. 1983. Cardiovascular effects of chronic barium ingestion. *In.:* Proc. 17th Ann. Conf. Trace Substances in Environmental Health, Vol. 17. University of Missouri Press, Columbia, MO. p. 155-164. (Cited in HEAST).

Schroeder, H. and M. Mitchener. 1975a. Life-Term Studies in Rats: Effects of Aluminum, Barium, Beryllium, and Tungsten. *J. Nutr.* 105:421-427. (Cited in HEA, 1984).

Schroeder, H. and M. Mitchener. 1975b. Life-Term Effects of Mercury, Methyl Mercury, and Nine Other Trace Metals on Mice. *J. Nutr.* 105:452-458. (Cited in HEA, 1984).

Sittig, M. 1991. *Handbook of Toxic and Hazardous Chemicals.*

Tarasenko, et al. 1987. (full reference not cited in IRIS).

U.S. EPA. *Drinking Water Regulations and Health Advisories.*

U.S. EPA. 1984. *Health Effects Assessment for Barium.* EPA/540/1-86/021.

U.S. EPA. *Health Effects Assessment Summary Tables (HEAST).*

U.S. EPA. *Integrated Risk Information System (IRIS).*

U.S. EPA, OERR. *CERCLA Compliance With Other Laws Manual Interim Final.* August, 1988.

U.S. EPA. 1986. *Quality Criteria for Water.* EPA 440/5-86-001.

Wones, R.G., et al. 1990. Lack of Effect of Drinking Water Barium on Cardiovascular risk factor. (Cited in IRIS).

BERYLLIUM

Use

Beryllium is a gray metal that is used as an alloy in numerous industries because of its light weight and high tensile strength. In the atomic energy field, it is used as a moderator in fission reactors and as a reflector to reduce leakage from the core (Sittig, 1991). Beryllium is alloyed with numerous other metals. As an alloy with copper, beryllium is used in machinery parts subjected to heavy wear or extreme vibration, in springs, in radar components and in non-sparking tools. As an alloy with nickel, beryllium is used on airplanes, in diamond drill-bit matrices, and in watch-balance wheels. Beryllium-bronze is used in switch parts, watch springs, diaphragms, shims, and bushings (Sittig, 1991)

Exposure to beryllium is generally associated with the milling and alloying processes and not in the mining of the beryl ore.

Chemical and Physical Properties

AW: 9.012 BP: 2970°C
SG: 1.85 at 20°C MP: 1278°C
Sol. (water): insoluble (except for beryllium salts)
Sol. (organics): dilute acid and alkali.

Fate and Transport

The majority of beryllium releases, most of which occurs as a result of coal combustion and milling processes, are to the atmosphere. Because these are releases of particulate, rather than dissolved beryllium, deposition is the most common fate. Generally, the ultimate destination of atmospheric beryllium is the soil (EPA, 1987). In the soil, beryllium tends to sorb to particulate matter in the relatively insoluble form of beryllium oxide.

When deposed or released to surface waters, the more commonly used beryllium compounds, most of which are water soluble, are hydrolyzed to beryllium hydroxide (ICF, 1985). Because beryllium hydroxide is relatively insoluble in the pH range of most surface waters, it remains stable and sorbs to any particulate matter present (ICF, 1985).

Pharmacokinetics

Beryllium is known to accumulate in the lungs of humans and laboratory animals after atmospheric exposure to elevated concentrations. Reeves, et al. (1967) showed that rats exposed to an atmospheric beryllium concentration of 35 $\mu g/m^3$ for 7 hours/day, 5 days/week for 72 weeks accumulated 13.5 µg in the lungs after 36 weeks of exposure. Examinations of human lung tissue revealed that beryllium concentrations in the lungs of occupationally exposed workers reach levels two to ten times as high as those in normal human lung tissues (EPA, 1987).

Ingested beryllium has, in some studies, been shown to be absorbed slightly through the gastrointestinal lining (less than 1 percent). However, Reeves (1965) exposed rats to beryllium in drinking water at an average daily ingestion concentration of either 6.6 or 66.6 µg Be. Sixty to ninety percent of the ingested beryllium was eliminated in the feces, indicating that an appreciable amount was ingested.

Absorbed beryllium accumulates primarily in the skeleton. Of the soft tissues, the liver and kidneys accumulate the most (EPA, 1987).

Human Toxicity

Noncarcinogenic Effects

Systemic Effects

Acute occupational exposure to atmospheric beryllium is known to cause lung disease. In a study of six fatal cases of beryllium poisoning, Frieman and Hardy (1970) reported that death occurred between 17 and 70 days after exposure. Interstitial pneumonitis was determined to be the cause of the fatalities.

Chronic exposure to beryllium can also result in lung disease. Hardy and Tabershaw (1946) reported that 5 of 17 workers studied in a fluorescent lamp manufacturing plant died from chronic beryllium exposure. The cause of death was noted to be an inflammation of cells within the alveoli.

It has also been noted that chronic exposure to beryllium can cause enlargement of the heart, liver and spleen; cyanosis; and kidney stone development (ICF, 1985).

Teratogenic and Other Developmental Effects

Three major studies were located in the available literature that provide inconclusive evidence as to the teratogenicity of beryllium. It appears as though no reproductive or teratogenic effects are caused by beryllium (EPA, 1987).

Mutagenic Effects

Beryllium has been proven to be mutagenic to cultured mammalian cells. Miyaki, et al. (1979) noted that Chinese hamster V79 cells, induced with beryllium chloride, were six times more likely to mutate than control V79 cells. The same results were noted by Hsie, et al. (1979) in Chinese hamster ovary cells.

Human lymphocyte cells are also known to mutate more frequently when exposed to beryllium compounds. Larramendy, et al. (1981) exposed human lymphocytes to beryllium sulfate in a single dose of 0.25 μg Be/ml. A six-fold increase in chromosomal aberrations was noted during cell division.

Carcinogenic Effects

Carcinogenicity case studies of occupationally exposed workers have been inconclusive. Of the studies performed, external factors were not appropriately taken into account. In most of the studies, the effects of cigarette smoking were not factored in but, when they were, no significant increase in tumors was noted (IRIS).

Studies performed on laboratory animals indicate that beryllium is carcinogenic. Schroeder and Mitchener (1975) reported a slightly significant increase in the incidence of unspecified cancerous growths in Long-Evans rats administered 5 ppm beryllium sulfate in drinking water for a lifetime.

In numerous studies, osteogenic sarcomas were induced in rabbits exposed to beryllium compounds via intravenous injection (IRIS).

Tumors have also been induced in Wistar rats through the intratracheal injection of metallic beryllium, beryllium-aluminum alloys, and beryllium oxide. Adenomas, adenocarcinomas, and malignant lymphomas were all noted in the lungs of the test rats (IRIS, 1990).

Ecotoxicity

Beryllium's toxicity to freshwater aquatic life appears to be affected by the amount of calcium carbonate in the water. Acute toxicity values for the Fathead Minnow changed from 150 μg/l in water with 20 mg/l calcium carbonate, to 20,000 μg/l in water with 400 mg/l calcium carbonate (ICF, 1985). From the limited data available, beryllium is thought to be mildly toxic to saltwater aquatic species.

Changes in skeletal growth were noted in poultry and livestock after soluble beryllium salts were added to their diets. Rachitis, a condition in which the long bones develop improperly, was noted to occur after the induction of 0.125 percent beryllium carbonate into the diet (IRIS).

Standards, Criteria and Guidelines

EPA Class B2 Carcinogen

Oral Slope Factor:	4.3×10^{0} (mg/kg/day)$^{-1}$
Chronic Oral RfD:	5.0×10^{-3} mg/kg/day
Subchronic Oral RfD:	5.0×10^{-3} mg/kg/day
MCL:	0.004 mg/L

AWQC: Acute: 130 µg/L (LOEL)
Chronic: 5.3 µg/L (LOEL)

BIBLIOGRAPHY

Frieman, D.G., and H.L. Hardy. Beryllium Disease: The Relation of Pulmonary Pathology to Clinical Course and Prognosis Based on the Study of 130 Cases from the U.S. Beryllium Case Registry. *Hum. Patho.* 1:25-44. (Cited in EPA, 1985).

Hardy, H.L. and I.R. Tabershaw. 1946. Delayed Chemical Pneumonitis Occurring in Workers Exposed to Beryllium Compounds. *Ind. Hyg. Toxicol.* 28:197-211. (Cited in EPA, 1987).

Hsie, A.W., et al. 1979. Quantitative Mammalian Cell Mutagenesis and a Preliminary Study of the Mutagenic Potential of Metallic Compounds. Karasch, N. Ed. *Trace Metals in Health and Disease*, NY, NY, Raven Press, page 55-69. (Cited in EPA, 1987).

ICF Clement. 1985. *Chemical, Physical and Biological Properties of Compounds Present at Hazardous Waste Sites.*

Larramandy, M.L., Popescu, N.C., and N.A. DiPaolo. 1981. Induction by Inorganic Metal Salts of Sister Chromatid Exchanges and Chromosomal Aberrations in Human and Syrian Hamster Cell Strains. *Environ. Mutagen.* 3:597-606. (Cited in EPA, 1987).

Miyaki. M., Akamatsu, N., Ono, T., and H. Koyama. 1979. Mutagenicity of Metal Rations in Cultured Cells from Chinese Hamster. *Mutat. Res.* 68:259-263. (Cited in EPA, 1987).

Reeves, A.L. 1965. The Absorption of Beryllium from the Gastrointestinal Tract. *Arch. Environ. Health.* 11:209-214. (Cited in EPA, 1987).

Reeves, A.L., and A.J. Vorwald. 1967. Beryllium Carcinogenesis: II, Pulmonary Deposition and Clearance of Inhaled Beryllium Sulfate in the Rat. *Cancer Res.* 27:446-451. (Cited in EPA, 1987).

Schroeder, H.A. and M. Mitchener. 1975. Life-Term Studies in Rats: Effects of Aluminum, Barium, Beryllium and Tungsten. *J. Nutr.* 105:421-427. (Cited in IRIS).

Sittig, M. 1991. *Handbook of Toxic and Hazardous Chemicals.*

U.S. EPA. *Drinking Water Regulations and Health Advisories.*

U.S. EPA. 1987. *Health Assessment Document for Beryllium.*

U.S. EPA. *Health Assessment Summary Tables (HEAST).*

U.S. EPA. *Integrated Risk Information System (IRIS).*

U.S. EPA, OERR. *CERCLA Compliance With Other Laws Manual Interim Final.* August, 1988.

U.S. EPA. 1986. *Quality Criteria for Water* EPA 440/5-86-001.

Vorwold, A.J. 1968. Biologic manifestations of toxic inhalants in monkeys. *In:* Use of Nonhuman Primates in Drug Evaluation, H. Vagtborg, Ed. Univ. of Texas Press, Austin, TX. p. 222-228. (cited in IRIS).

CADMIUM

Use

Elemental cadmium is a soft white metal similar to lead and zinc in texture and in other physical properties.

Cadmium is obtained as a byproduct during the production of zinc. Commercially, cadmium is used in the metal plating industry; as a stabilizer in paints, pigments, and plastics; and as an energy storage medium in batteries. It is also used in pesticides, as an alloy additive, and in chemical reagents. Cadmium may escape into the air from zinc, lead, or copper smelters. Naturally occurring levels of cadmium in surface and ground water normally fall in the range of 1-10 g/liter (EPA, 1985).

Physical and Chemical Properties

AW: 112.41	BP: 765°C
SG: 8.642	MP: 321°C
	VP: 1 mmHg at 394°C

Sol. (water): metal is insoluble, salts of metal are soluble
Sol. (organics): variable

Fate and Transport

The primary vehicle for cadmium exposure in a non-occupational setting is through the ground water. Cadmium is relatively mobile in aquatic environments and sorbs to organic material found in soils (EPA, 1984). It is thought to be transported slowly by ground water, but no comprehensive studies have been performed in this regard. High cadmium levels are often found in ground water surrounding smelting and plating facilities (Sittig, 1991). Occupationally, workers can be exposed to cadmium in the form of dust or fumes.

Pharmacokinetics

Cadmium is absorbed moderately in the lungs but quite poorly in the gastrointestinal tract (1 to 6 percent in both humans and animals). The primary excretory route for absorbed cadmium is the urine (ATSDR, 1989). Urinary excretion is slow, however, and cadmium has a strong tendency to accumulate in the body (mostly in the liver and renal cortex) over time in exposed humans and in animals (cadmium binds tightly to the protein metallothionein or its cellular components). The half lives of cadmium and its compounds in the body range from 17 to 38 years (ATSDR, 1989). Measurements of alveolar absorption in rats indicate 60 to 70 percent absorption over time. Calculations based on increased body burden in smokers compared to that in nonsmokers suggest that respiratory absorption in humans is probably about 30 to 60 percent (ATSDR, 1989). The absorption of cadmium following oral administration of laboratory animals, and presumably humans, is not a simple process and is modified by many factors including chemical form solubility dose, age, diet, and by the presence of other metals. Small quantities of cadmium may be absorbed through the skin but

dermal absorption is not normally significant relative to total cadmium absorption (ATSDR, 1989). In general, soluble compounds such as $CdCl_2$ are better absorbed and are more toxic than highly insoluble compounds such as CdS. (ATSDR, 1989).

Human Toxicity

Noncarcinogenic Effects

Systemic Effects

In the case of severe intoxication, sensory disturbances, liver injury, and convulsions may occur. In fatal intoxications, this is followed by shock and/or renal failure and cardiopulmonary depression (EPA, 1985). Exposure to concentrations of 40 to 50 mg/m^3 for 1 hour and 9 mg/m^3 for 5 hours has resulted in fatalities. LD_{50} values in animals exposed to cadmium oxide fumes range from 500 to 15,000 mg/m^3 minute (ATSDR, 1989). Acute oral LD_{50} values in animals for cadmium oxide and common cadmium salts range from 50 to 350 mg/kg (ATSDR, 1989).

Renal effects: The kidney is generally recognized as the most sensitive tissue to low-level cadmium exposure, the major effect being impaired tubular reabsorption. Rats receiving water containing cadmium at 30 or 100 mg/liter developed significant ($p<0.05$) proteinuria after 6 weeks of exposure (EPA, 1985). Various studies indicate that tubular dysfunction does not generally occur in humans until a renal cortical concentration of approximately 200 µg/g wet weight is reached (ATSDR, 1989). Using this figure, it was estimated that a daily oral intake of 352 µg/day over 50 years would not exceed the critical level of cadmium in the renal cortex. A more recent study in which epidemiological studies were reviewed, however, concluded that an average oral exposures of about 200 µg/days will cause tubular proteinuria in about 10 percent of an exposed population by age 45 (ATSDR, 1989). It was also estimated that 10 percent of a working population exposed via inhalation to 50 $\mu g/m^3$ would develop proteinuria in 10 years. (ATSDR, 1989).

Hepatic effects: The next highest tissue levels of cadmium are found in the liver. While structural changes were observed following cadmium exposure in food and water to rats and rabbits, clinical tests revealed normal hepatic function. There is little evidence for liver dysfunction in chronically exposed human populations but hepatic levels may serve as a useful index of exposure and a predictor of future renal dysfunction (ATSDR, 1989).

Cardiovascular effects: Certain animal studies have indicated that increases in average systolic blood pressure occur following exposure to cadmium acetate in the drinking water (0.5 mg/kg/day); not all investigations have succeeded in confirming these findings and other factors may confound the effects of

cadmium (ATSDR, 1989). The role of cadmium is human hypertension is uncertain (ATSDR, 1989).

Pulmonary effects: Inhalation exposure to high levels of cadmium oxide fumes is intensely irritating to respiratory tissues (ATSDR, 1989).

Gastrointestinal effects: In humans, the symptoms of cadmium toxicity following acute oral exposure include nausea, vomiting, diarrhea, abdominal pain, and salivation (ATSDR, 1989).

Other systemic effects: Weak evidence exists indicating skeletal effects in humans and animals exposed chronically to cadmium. Studies revealed that relatively low doses of cadmium can alter the immune response in animals (at very low renal cadmium concentrations ranging from 0.3 to 6.0 μg/g) (ATSDR, 1989). Parenteral injection of cadmium has been observed to cause severe acute pathological changes in the gonads of animals (ATSDR, 1989). Exposure by injection of male rats with 2.2 mg/kg of $CdCl_2$ resulted in swelling and inflammation of testes, followed by necrosis and atrophy, in several studies. Another common effect in cadmium-exposed animals is anemia (ATSDR, 1989).

Teratogenic and Other Developmental Effects

Sutou, et al. (1980) administered cadmium at 0, 0.1, 1.0, and 10.0 mg/kg/day (as $CdCl_2$) orally to male and female adult rats for 6 weeks. Males and female were mated for 3 weeks, and cadmium was administered during the mating period. Pregnant females were given cadmium during the gestation period. The number of total implants and live fetuses decreased significantly in the 10 mg/kg group, and the number of resorbed fetuses was markedly increased. Fetuses showed decreased body weight, and delayed ossification of the sternebrae and caudal vertebrae. Ahokas, et al. (1980) observed, in a rat drinking-water-study, fetal growth retardation in animals whose dams were exposed to 100 mg cadmium/L but not in those exposed to 0.1 or 10 mg cadmium/L during gestation. The most common finding is the decreased weight of offspring, with ingestion exposure, usually without significant teratogenic or developmental effects (ATSDR, 1989). Cadmium exposure has not been observed to cause teratogenic or other developmental effects in exposed humans (ATSDR, 1989).

Mutagenic Effect

Studies to assess the mutagenic activity of cadmium, in *Salmonella typhimurium, E. coli,* and yeast, have been inconclusive (ATSDR, 1989). Recombination assays in *Bacillus subtilis* have yielded weak positive responses (ATSDR, 1989). Cadmium has been shown to be mutagenic both in the mouse lymphoma assay and in the Chinese hamster cell assay (ATSDR, 1989).

Chromosomal aberration studies on human lymphocytes from exposed workers and in human and animal cells treated with cadmium *in vitro* have produced conflicting results (ATSDR, 1989).

Carcinogenic Effects

EPA has evaluated the weight of evidence on the carcinogenicity of cadmium and has concluded that cadmium is a probable human carcinogen (Group B1) by inhalation (ATSDR, 1989/IRIS). An occupational study of smelter workers by Thun, et al. (1985) revealed a two-fold excess risk of lung cancer but confounding factors could not be ruled out. Wistar rats exposed to cadmium chloride developed significant increases in lung tumors (Takenaka, et al., 1983). No sufficient data exists to consider cadmium as carcinogenic by the oral route, nor is there evidence that cadmium, via the dermal route, is carcinogenic to either animals or humans.

Ecotoxicity

The acute LC_{50} values for cadmium exposure in freshwater fish and invertebrates generally range from 100 to 1,000 µg/liter. Salmoids, being very sensitive, would be at the lower end of this range. Saltwater species appear to be, in general, 10-times more tolerant to the acute effects of cadmium than freshwater species (ICF, 1985). Cadmium is strongly accumulated by all organisms (ATSDR, 1989). Bioconcentration factors (BCFs) for cadmium in freshwater range from 164 to 4,190 for invertebrates and from 3 to 2,213 for fish. BCFs for saltwater invertebrates range from 5 to 3,160 (EPA, 1986).

Freshwater acute values for cadmium are available for species in 44 genera and range from 1.0 µg/L for rainbow trout to 28,000 µg/L for mayflies. Chronic tests conducted for cadmium on 12 freshwater fish species and 4 invertebrate species revealed chronic values ranging from 0.15 µg/L for *Daphnia magna* to 156 µg/L for the Atlantic salmon. Acute-chronic ratios, available for eight species, range from 0.9021 for the Chinook salmon to 433.8 for the flagfish (EPA, 1986). Freshwater aquatic plants are affected by cadmium at concentrations ranging from 2 to 7,400 µg/L. The major toxic effect observed in freshwater aquatic plants was growth reduction.

Saltwater acute values for cadmium in five species of fish range from 577 µg/L for Atlantic silverside to 114,000 µg/L for juvenile mummichog. Invertebrate acute values (30 species) range from 15.5 µg/L for a mysid to 135,000 µg/L for an oligochaete worm. Acute toxicity of cadmium usually increases as salinity decreases. Chronic cadmium exposure has been shown to significantly affect the growth of bay scallops at 78 µg/L and the reproduction of certain copepods at 44 µg/L (EPA, 1986).

Standards, Criteria and Guidelines

EPA Class B1 Carcinogen

Oral Slope Factor:	NA
Inhalation Slope Factor:	$6.3x10^{0}$ $(mg/kg/day)^{-1}$
Chronic Oral RfD:	1.0×10^{-3} mg/kg/day (food)
	5.0×10^{-4} mg/kg/day (water)
Chronic Inhalation RfD:	Currently under review by EPA
Subchronic Oral RfD:	5.0×10^{-4} mg/kg/day
Subchronic Inhalation RfD:	NA
MCL:	0.005 mg/l
AWQC:	Water and Fish Consumption - 10 µg/l
	Fish Consumption - NA

BIBLIOGRAPHY

Agency for Toxic Substances and Disease Registry, U.S. Public Health Service, *Toxicological Profile for Cadmium*, ATSDR/TP-88/08, March 1989.

Ahokas, R.A., P.U. Dilts and E. B. LaHage, Cadmium Induced Fetal Growth Retardation: Protective Effect of Excess Dietary Zinc, 1980, *Am. J. Gynecol.* (cited in EPA, 1985).

ICF Clement Associates, *Chemical, Physical, and Biological Properties of Compounds Present at Hazardous Waste Sites*, September, 1985.

Sittig, Marshall, *Handbook of Toxic and Hazardous Chemicals*, 1991.

Sutou, S., K. Yamamoto, H. Sendota and M. Sugiyama, Toxicity, Fertility, Teratogenicity and Dominant Lethal Tests in Rats Administered Cadmium Subchronically. III, Fertility, Teratogenicity and Dominant Lethal Test, 1980, *Ecotoxicol. Environ. Safety*, 4:51-56, (Cited in EPA, 1985).

Takenaka, S., H. Oldiges. H. Konig, D. Hochrainer and G. Oberdoerster, Carcinogenicity of Cadmium Aerosols in Wistar Rats, 1983, *J. National Cancer Inst.*, 70: 367-373, (Cited in IRIS).

Thun, M.J., T.M. Schnorr, A.B. Smith and W.E. Halperin, Mortality Among a Cohort of U.S. Cadmium Production Workers: An Update, 1985, *J. Natl. Cancer Inst.*, 74(2): 325-333, (Cited in IRIS).

U.S. EPA, *Drinking Water Regulations and Health Advisories.*

U.S. EPA, *Health Advisory for Cadmium*, 1985.

U.S. EPA, Office of Water Regulations and Standards, *Quality Criteria for Water*, 440/5-86-001, May 1, 1986.

U.S. EPA, *Acute Toxicity Handbook of Chemicals to Estuarine Organisms*, EPA/600/8-87/017, April 1987 (Env. Res. Lab/Office of R and D) Gulf Breeze, Florida.

U.S. EPA, *Health Effects Assessment for Cadmium*, EPA 540/1-86/038, 1984.

U.S. EPA, *Integrated Risk Information System (IRIS).*

U.S. EPA, OERR. *CERCLA Compliance With Other Laws Manual Interim Final.* August, 1988.

CHROMIUM

Use

Chromium and chromium compounds are used in stainless and alloy steels, refractory products, tanning agents for leather, pigments, electroplating, catalysts, and in corrosion resistant products (ACGIH, 1991).

Chemical and Physical Properties

AW: 51.996 BP: 2672°C
SG: 7.20 at 28°C MP: 1857 ±20°c
Sol. (water): insoluble, some compounds are soluble.

Fate and Transport

Chromium (VI) is soluble in water and is transported easily in ground water. It may exist in aquatic systems as water soluble, complex anions, and may persist for long periods of time (EPA, 1984a). Chromium (VI) may react with organic matter in the soil or surface waters to form trivalent chromium, therefore chromium (VI) may exhibit a shorter lifespan in soils with high organic content (EPA, 1984a).

The primary means by which chromium (III) is transported out of soils and surface waters is through aerosol formation and runoff. It is also hydrolyzed to chromium hydroxide. Leaching does not generally occur with chromium (III) because it is generally present as insoluble chromium trioxide.

Pharmacokinetics

The amount of ingested chromium (VI) and (III) absorbed is estimated to be 5 percent and 3 percent respectively. Donaldson and Barreras (1966) fed $Na_2{}^{51}Cr(VI)0_4$ to rats and humans and $^{51}Cr(III)Cl_3$ to humans. Based on mean urinary excretion of $^{51}Cr(VI)$, absorption was estimated to be 2.1 percent in humans. In rats, 2 percent of the administered dose was absorbed, based on fecal excretion of $^{51}Cr(VI)$. Based on fecal excretion of $^{51}Cr(III)$, absorption was estimated to be 0.4 percent in humans. However, when $Na_2{}^{51}Cr(VI)0_4$ was administered introduodenally (in humans) or intrajejunally (in rats), absorption was estimated to be 50 and 25 percent, respectively. When $^{51}Cr(III)Cl_3$ was administered introduodenally, absorption was not appreciably changed. A study by Langard, et al. (1978) indicates that water-soluble chromium (VI) is absorbed rapidly via inhalation. Rats were exposed to zinc chromate dust at a level of 7.35 mg/m^3. After 0, 100, 250, and 350 minutes of exposure, the concentrations of chromium in the blood (µg/ml) were 0.007, 0.024, 0.22, and 0.31, respectively. Chromium (III) is absorbed slowly via inhalation. Baetjer et al. (1959) administered $^{51}Cr(III)Cl_3$ to guinea pigs intratracheally. Only 4 percent of the administered dose was detected in the blood and tissues 10 minutes post-treatment; 69 percent remained in the lungs. 45, 30, and 12 percent of the administered dose was detected in the lungs 1, 30, and 60 days post-treatment, respectively.

Human Toxicity

Noncarcinogenic

Systemic Effects

Bloomfield and Blum (1928) examined 23 men from six chromium plating plants in the U.S. Fourteen of the workers typically spent 2-7 hours/day over vats of chromic acid, which generated airborne hexavalent chromium ranging from 0.12-5.6 mg/m^3. These men experienced nasal tissue damage, including perforated septa, ulcerated septa, chrome holes, nosebleed, and inflamed mucosae. The nine remaining workers not directly exposed to chromium vapors had only inflamed mucosae.

Mackenzie, et al. (1958) exposed groups of rats, both male and female, to potassium dichromate (0-25 ppm of hexavalent chromium) in drinking water for 1 year. No effects were observed at any level of treatment. Pertinent data regarding subchronic exposure of animals to hexavalent chromium via inhalation were not located in the literature (EPA, 1984a).

Ivankovic and Preussman (1975) exposed groups of 60 male and female rats to 0, 1, 2, or 5 percent $Cr(III)_2O_3$ in baked bread, 5 days/week for 600 feedings. The average total amounts of ingested $Cr(III)_2O_3$ were given as 0, 360, 720, and 1800 g/kg bw. No adverse effects were observed at any dose level.

Teratogenic and Other Developmental Effects

The literature available on teratogenic effects resulting from ingestion of chromium is limited. However, several forms of chromium (including chromium (III)), when administered to pregnant rats by stomach intubation in the form of GTF (obtained from yeast), have been found to cross the placental barrier and be recovered by the fetus (EPA, 1985).

Mutagenic Effects

Compounds of both chromium (III) and chromium (VI) increase noncomplementary nucleotide incorporation into DNA with chromium (VI) being effective at lower doses. Exposure of cells from rat liver and kidney to chromium (VI) leads to increased cross-linking in DNA. Positive Ames tests for chromium (VI) have been reported; however chromium (III) exerted no effect at relatively high concentrations (presumably because of its inability to penetrate cells), (EPA, 1985).

Carcinogenic Effects

Data regarding the carcinogenicity of inhaled chromium (VI) is well established for occupational exposure in humans. The effects are observed only in the respiratory passages and in the lungs (EPA, 1985).

Numerous epidemiological studies indicate that various forms of chromium (VI) cause lung cancer as a result of chronic exposure (Machle and Gregorius, 1948). It has been estimated that workers in the chromate pigment industry who had developed lung cancer were exposed to 0.01 to 0.15 mg/m^3 of water soluble chromium and 0.1 to 0.58 mg/m^3 of water insoluble chromium. From subsequent studies, it appears that water insoluble compounds of chromium (VI) resulted in the increase in lung cancer (ACGIH, 1984).

There is inadequate evidence to determine whether or not oral exposure to chromium (III) can lead to cancer. Rats exposed to chromium (III) at 293, 586, or 1,4676 mg/kg/day in the diet (administered as chromium oxide pigments) for 2 years, displayed no increase in the tumor rates over that of the control animals (EPA, 1985).

Ecotoxicity

Chromium is an essential nutrient and is accumulated in a variety of aquatic and marine biota, especially benthic organisms, to levels much higher than in ambient water. Levels in biota, however, are usually lower than levels in the sediments. Passage of chromium through the food chain can be demonstrated (ICF, 1985); however, chromium concentrations are usually higher in the lower trophic levels; biomagnification through the food chain has not been reported (Eisler, 1986). The food chain appears to be a more efficient pathway for chromium uptake than direct uptake from seawater (ICF, 1985). Water hardness, temperature, dissolved oxygen, species, and age of the test organism all modify the toxic effects of chromium on aquatic life. Chromium (III) appears to be more acutely toxic to fish than chromium (VI), yet the reverse is true in long-term chronic exposure studies (ICF, 1985). None of the plants normally used as food or animal feed are chromium accumulators. Chromium absorbed by plants tends to remain primarily in the roots and is poorly translocated to the leaves. There is little tendency for chromium to accumulate in food chains in the trivalent inorganic form. Organic chromium compounds, about which little is known, can have significantly different bioaccumulation tendencies (ICF, 1985).

Chromium diet concentrations of 5.1 mg Cr(VI) and 10.0 mg Cr(III) per kg food are harmful to wildlife (Eisler, 1986).

Standards, Criteria and Guidelines

EPA Class A Carcinogen (Hexavalent Chromium)

Oral Slope Factor:	NA
Chronic Oral RfD:	5.0×10^{-3} mg/kg/day (VI)
Subchronic Oral RfD:	2.0×10^{-2} mg/kg/day (VI)
MCL:	0.1 mg/L (total)
AWQC:	Acute: 16 µg/L
	Chronic: 11 µg/L

BIBLIOGRAPHY

American Conference of Governmental Industrial Hygienists (ACGIH). 1991. *Documentation of the Threshold Limitation Values.*

Baetjer, A.M., et al. 1959. The distribution and retention of chromium in men and animals. *Arch. Ind. Health* 20:136-150. (Cited in EPA, 1984b).

Bloomfield, J.J. and W. Blum. 1928. Health Hazards in Chromium Plating. *Public Health Rep.* 43:2330-2351. (Cited in EPA, 1984a).

Donaldson, R.M. and R.F. Barreras. 1966. Intentional Absorption of Trace Quantities of Chromium. *J. Lab Clinic. Med.* 68:484-493. (Cited in EPA, 1984a).

Furst, A., et. al. 1976. Tumorigenic activity of lead chromate. *Cancer Res.* 36:1779-1783. (cited in IRIS).

Eisler, R. 1986. Chromium hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish Wildl. Serv. Biol. Rep. 85 (1.6) 60 pp.

ICF Clement. 1985. *Chemical, Physical and Biological Properties of Compounds present at Hazardous Waste Sites.*

Ivankovic, S. and R. Preussman. 1975. Absence of toxic and carcinogenic effects after administration of high doses of chromic oxide pigment in subacute and long term feeding experiments in rats. *Food Cosmet. Toxicol.* 13:317-351. (cited in IRIS).

Langard, S., N.J. Gundersen, D.L. Tsalev and B. Glyseth. 1978. Whole Blood Chromium Level and Chromium Excretion in the Rat After Zinc Chromate Inhalation. *Acta. Pharmacal. Toxicol.* 42:142-149. (Cited in EPA, 1984a).

Lindberg, E. and G. Hedenstierna. 1983. Chrome plating: Symptoms, findings in the upper airways, and effects on lung function. *Arch. Environ. Health.* 38:367-374. (cited in HEAST).

Machle, W. and F. Gregorius. 1948. Cancer of the respiratory system in the United States chromate-producing industry. *Public Health Rep.* 63(35):1114-1127. (cited in IRIS).

Machle, W. and F. Gregorius. 1948. Cancer of the Respiratory System in the United States chromate-producing industry. *Public Health Rep.* 63(35):114-1127. (cited in IRIS).

Mackenzie, R.D., R.A. Anwar, R.U. Byerrum, and C.A. Hoppert. 1959. Absorption and Distribution of ^{51}Cr in the Albino Rat. *Arch. Biochem. Biophys.* 79:200-250. (Cited in EPA, 1984a).

Sittig, M. 1991. *Handbook of Toxic and Hazardous Chemicals.*

U.S. EPA. *Drinking Water Regulations and Health Advisories.*

U.S. EPA. 1985. *Health Advisory for Chromium, Office of Drinking Water.*

U.S. EPA. 1984a. *Health Effects Assessment for Hexavalent Chromium.* EPA 540/1-86/019.

U.S. EPA. 1990. *Integrated Risk Information System.*

U.S. EPA. *Health Effects Assessment Summary Tables (HEAST).*

U.S. EPA. 1984b. *Health Effects Assessment for Trivalent Chromium.* 2 EPA 540/1-86/035.

U.S. EPA, OERR. *CERCLA Compliance With Other Laws Manual Interim Final.* August, 1988.

LEAD

Use

Lead is a heavy metal that exists in three oxidation states (0, +2, and +4). In addition to their natural occurrence, lead and its compounds may enter and contaminate the global environment at any stage during mining, smelting, processing, and use. The annual increase in lead consumption in the United States during the 10-year period from 1962-1971 averaged 2.9 percent, largely due to increased demands for electro-chemical batteries and gasoline additives (EPA, 1984). Nonindustrial sources that may contribute to the possibility of ingestion of lead by man include the indoor use of lead-bearing paints and plasters, improperly glazed earthenware, lead fumes or ashes produced in burning lead battery casings, and exhaust from internal combustion engines (EPA, 1984).

Chemical and Physical Properties

AW: 207.19 BP: 1,704°C
SG: 11.35 at 20°C MP: 327.5°C
Sol. (Water): Insoluble
Sol. (Inorganics): $HN0_3$, hot H_2S0_4

Fate and Transport

Lead is artificially introduced into the environment primarily through the combustion of lead-containing fossil fuels and from lead mining operations (EPA, 1984). Lead fumes undergo decomposition when exposed to light. As a result, fumes that are present around gas stations and in heavily travelled areas are not a significant avenue of contamination (EPA, 1989). Particulate lead, carried in the atmosphere, is removed by either wet or dry deposition. Rainfall is not as significant in the deposition of lead particles as would be expected (EPA, 1984).

The transport of lead in ground water and surface water is highly variable based on its oxidation state. In polluted waters, organic complexation of lead is the primary factor in the determination of toxicity. Lead is adsorbed strongly to organic materials in soils but is not easily absorbed by living plants (EPA, 1984).

Pharmacokinetics

It has been estimated that, in man, approximately 8 percent of the lead ingested daily is absorbed. Absorption of lead consumed by humans after a 6-hour fast was increased up to 8-fold when compared with lead consumed with food. Similar effects were observed in dietary studies of mice given a dose of 3 µg Pb/kg-bw, but not at much higher doses (2,000 µg Pb/kg bw) (EPA, 1984). Numerous dietary factors influence the absorption of lead from the gastrointestinal tract. Lead absorption has been demonstrated to be enhanced by low dietary calcium or iron, high dietary fat, or low or high protein. Four baboons exposed to lead

aerosols (Pb_3O_4) of varying particle size for 4 weeks showed that absorption was faster for 1.6 μm particles than for more fine particles (0.8 μm) (EPA, 1984).

In humans, it appears as though hemoglobin and hemo-proteins are affected by lead more so than any other organ or system (EPA, 1984). At levels of 0.4 μg Pb/ml blood in adults, the amount of hemoglobin and hemo-proteins produced is decreased.

Human Toxicity

Noncarcinogenic

Systemic Effects

The majority of the studies concerned with the effects of lead exposure in humans are based on blood lead levels, not ambient lead levels (EPA, 1984). Decreased hemoglobin production is seen at low blood lead levels of 0.5 μg/ml blood in children.

Chronic exposure of rats to lead acetate produced slight effects on conduction tissue excitability, systolic blood pressure, and cardiac ATP concentrations. This study was performed over a period of 20 weeks on rats given 5 mg Pb/L water in their drinking water (EPA, 1984).

Teratogenic and Other Developmental Effects

Postnatal developmental delays have been reported in pups from rats that received 50-250 mg Pb/liter in drinking water throughout gestation (EPA, 1984). Effects on reproductive parameters were noted in rats and mice in a three-generation study with 25 ppm lead (from an unspecified soluble lead salt) in drinking water. In this study, environmental concentrations of other metals were minimized (EPA, 1984). In high doses, lead compounds have been used to induce abortions. Oliver (1911) noted that the miscarriage rate among British women occupationally exposed to lead was elevated. Several other studies have reported that increases in spontaneous abortions, premature delivery, and early membrane rupture have been associated with lead exposure.

In one study, groups of 60-90, 21-day-old female CD rats were administered a semipurified, nutritionally adequate, virtually lead-free diet. Lead acetate was administered in deionized drinking water at concentrations of 0, 0.5, 5, 50, or 250 mg Pb/liter of water. The treated females were mated with untreated males after 6-7 weeks and were continued on treatment throughout gestation and lactation. There were no treatment-related differences in food or water consumption between the various treatment groups; however, body weights of offspring were depressed at the two highest doses. Sexual maturation, as measured by the time of vaginal opening, was delayed in a dose-dependent

manner, with effects observed at concentrations 25 mg Pb/liter or greater (EPA, 1984).

Mutagenic Effects

DiPaolo, et al. (1978) noted that lead acetate induces cell transformation in Syrian hamster embryo cells and increases the incidence of simian adenovirus induction.

Grandjean, et al. (1983) discovered a relationship between sister-chromatid-exchange and lead exposure in workers.

Carcinogenic Effects

An increase in the incidence of renal tumors was observed in rats exposed to 1000 ppm and 2000 ppm in the diet for 2 years (Azar et al., 1973).

Similar results were observed when Kasprzak, et al. (1985) orally administered a dose of 8500 ppm Pb, as lead subacetate, per day to Sprague-Dawley rats for 79 weeks. Forty-four percent of the treated rats developed renal tumors; four of twenty-nine rats developed adenocarcinomas and the remaining nine developed adenomas. In a similar study, Koller, et al. (1986) administered 2600 ppm Pb, as lead acetate, in drinking water to Sprague-Dawley rats for 76 weeks. Eighty-one percent developed renal tubular carcinoma.

Dietary lead acetate administered in doses of 3-4 mg/day, 500-2000 mg/kg diet or 1 percent in the diet have produced renal tumors in Wistar rats (EPA, 1984). In a separate study, it was shown that a lead acetate produced renal carcinomas or adenomas in Swiss mice and several other rodents.

From available studies, it appears as though inorganic leads are the cause of any carcinogenic effects seen in humans or animals.

Ecotoxicity

Chronic toxicity studies of lead in *Daphnia magna* indicate that water hardness effects lead toxicity. The daphnids were nearly 11 times more sensitive to lead in soft water than in hard water. The chronic toxicity value of lead nitrate in water with a hardness of 52 mg/liter as $CaC0_3$ is 12.26 µg/liter. An early life stage test was conducted on the highly sensitive rainbow trout (*Salmo gairdneri*). For trout raised in water with a hardness of 28 mg/l $CaCO_3$, a chronic toxicity value of 18.80 mg/l was generated. The only chronic study located concerning saltwater species was conducted on mysid shrimp (*Mysidopsis bahia).* The results indicate that this small crustacean is highly sensitive to lead nitrate, yielding a chronic toxicity value of 25.08 µg/liter. The aforementioned chronic values are decisive in showing that lead nitrate is highly toxic to freshwater and saltwater aquatic life (EPA, 1984).

Although adverse effects of lead have been documented for avian species (50 to 75 mg Pb(II)/kg BW and 28 mg organolead/kg BW), data for toxic effects of lead to mammalian wildlife are lacking (Eisler, 1988).

Standards, Criteria and Guidelines

EPA Class B2 Carcinogen

Oral Slope Factor:	No slope factor derived by Carcinogen Assessment Group
Chronic Oral RfD:	NA/no threshold
Subchronic Oral RfD:	NA
MCL:	0.015 mg/L (action level)
AWQC:	Acute: 83 µg/L
	Chronic 3.2 µg/L (hardness dependent)

BIBLIOGRAPHY

Azar, A., et al. 1973. Review of lead studies in animals carried out at Haskell Laboratory-Two year feeding study and response to hemorrhage study. In: Barth, D. et al. *Environmental Health Aspects of Lead.* Proceedings International Symposium; October 1972; Amersterdam, The Netherlands. Commission of the European Communities, Luxemberg p. 199-208. (cited in IRIS).

DiPaolo, J.A., R.L. Nelson, and B.C. Casto. 1978. *In Vitro* Neoplastic Transformation of Syrian Hamster Cells by Lead Acetate and its Relevance to Environmental Carcinogenesis. *Br. J. Cancer.* 38: 452-455. (Cited in IRIS).

Eisler, R. 1988. Lead hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish Wildl. Serv. Biol. Rep. 85 (1.14). 134 pp.

Grandjean, P., H.C. Wulf, and E. Neibuhr. 1983. Sister-Chromatid-Exchange in Response to Variations in Occupational Lead Exposure. *Environ. Res.* 32: 199-204. (Cited in IRIS).

Kasprzak, K.S., K.L. Hoover, and L.A. Poirier. 1985. Effects of Dietary Calcium Acetate on Lead Subacetate Carcinogenicity in Kidneys of Male Sprague-Dawley Rats. *Carcinogenesis.* 6(2): 279-282, (Cited in IRIS).

Koller, L.D., N. I. Kerkvliet, and J.H. Exon. 1986. Neoplasia Induced in Male Rats Fed Lead, 1990 Acetate, Ethyl Urea and Sodium Nitrate. *Toxicol. Pathol.* 13: 50-57. (Cited in IRIS).

Oliver, T. 1911. Lead Poisoning and the Race. *Br. Med. J.* 1: 1096-1098. (Cited in EPA, 1984.

Sittig, M. 1991. *Handbook of Toxic and Hazardous Chemicals.*

U.S. EPA. 1986. *Air Quality Criteria for Lead*, June 1986 and Addendum. EPA 600/8-83-028F. (Cited in HEAST).

U.S. EPA. *Drinking Water Regulations and Health Advisories.*

U.S. EPA. 1984. *Health Effects Assessment for Lead*, EPA 540/1-86/055.

U.S. EPA. *Health Effects Assessment Summary Tables (HEAST).*

U.S. EPA. *Integrated Risk Information System (IRIS).*

U.S. EPA, OERR. *CERCLA Compliance With Other Laws Manual Interim Final.* August, 1988.

U.S. EPA. 1986. *Quality Criteria for Water.* EPA 440/5-86-001.

MANGANESE

Use

Manganese is used primarily as an alloy in steel and iron manufacturing. Manganese compounds are used in the manufacture of dry cell batteries, paints, varnishes, dyes, inks, fireworks, fertilizers, and disinfectants. Organic manganese compounds have been tested as potential supplemental anti-knock agents in gasolines (Sittig, 1991).

Chemical and Physical Properties

AW: 54.938
SG: 7.20
Sol. (water): decomposes
Sol. (organics): insoluble

BP: 1962°C
MP: 1244°C
VP: 1 mmHg at 1292°C

Fate and Transport

Manganese occurs most often in the +2, +4 and +7 valence states. Elemental manganese, as well as manganese compounds, are present in the atmosphere as a result of natural processes.

In the atmosphere, manganese can be present in particulate form and, as such, it is susceptible to photo-chemical and thermal reactions (EPA, 1984). Manganese reacts with SO_2 and NO_2 and is removed from the atmosphere most effectively through wet and dry deposition (EPA, 1984).

In aquatic media, the fate of manganese is effected primarily by the amount of dissolved oxygen present and by the acidity of the water. In aerobic waters, manganese forms MnO_2 and Mn_3O_4 which either remain suspended or deposit to the sediments. The residence time of insoluble manganese compounds is known to be as much as 300 years (EPA, 1984).

In soils, the solubility of manganese is increased with low Ph and with high concentrations of chlorides, nitrates, or sulfates. Under these conditions, manganese is transported readily and is absorbed rapidly by plants (ICF, 1985).

Pharmacokinetics

Absorption of manganese occurs primarily in the gastrointestinal tract and is controlled homeostatically by the amount of manganese already present in the body. Under normal conditions, approximately 3 percent of ingested manganese is absorbed. Anemia victims appear to absorb more than twice that amount (EPA, 1984). Manganese absorption appears to be competitive with iron absorption.

Inhalation studies indicate that small manganese particles are absorbed in the lungs by the alveoli and are excreted within 4 days. Approximately 40-70 percent of absorbed manganese is excreted in the feces (EPA, 1984).

Human Toxicity

Noncarcinogenic Effects

Systemic Effects

Orally administered manganese appears to cause minimal toxic effects in humans (ICF, 1985). The World Health Organization (WHO, 1973) reviewed several investigations which studied the effects of average daily consumption of concentrations of manganese ranging from 2 to 8.8 mg/Mn/day in adult diets. Levels from 8 to 9 mg/day were determined to be "perfectly safe". Reference doses (RfDs) were based on these studies, with a NOAEL of 0.14 mg/kg/day.

In one chronic ingestion study, Kawamura, et al. (1941) reported that 14.3 mg Mn/L drinking water causes lethargy, spasms, tremors, and mental disturbances. Both chronic inhalation and ingestion of manganese appear to effect the central nervous system most predominantly.

Teratogenic and Other Developmental Effects

Chronic manganese poisoning has been shown to cause depressed reproductive function in male and female laboratory animals. Penalver (1955) reported that oral exposure to manganese causes impotency in humans. Mandzgaladze (1967) reported that manganese exposure causes an increase in still births and spontaneous abortions in humans.

Mutagenic Effects

Manganese has been reported to be mutagenic to *Salmonella* strains and *E. coli.* Casto, et al. (1979) reported that manganese was moderately effective in enhancing viral transformation in Syrian hamster embryo cells.

Carcinogenic Effects

Manganese compounds, such as manganese chloride, manganese acetylacetonate, and manganese dioxide, caused an increased incidence of injection site tumors in rats but, EPA has determined that these results cannot be extrapolated to include elemental manganese (IRIS). No increase in lymphosarcomas and fibrosarcomas were noted by Furst (1978) in rats orally exposed to manganese powder.

Ecotoxicity

Data regarding the toxicity of manganese to aquatic organisms were not located in the available literature.

Standards, Criteria and Guidelines

EPA Class D Carcinogen

Oral Slope Factor:	NA
Chronic Oral RfD:	5.0×10^{-3} mg/kg/day (water)
	1.4×10^{-1} mg/kg/day (food)
Subchronic Oral RfD:	5.0×10^{-3} mg/kg/day (water)
	1.4×10^{-1} mg/kg/day (food)
MCL:	NA
AWQC:	NA

BIBLIOGRAPHY

American Conference of Governmental Industrial Hygienists. 1984. *Documentation of Threshold Limit Values.*

Casto, B.C., J. Meyers, and J.A. DiPaolo. 1979. Enhancement of Viral Transformation for Evaluation of the Carcinogenic or Mutagenic Potential of Inorganic Metal Salts. *Cancer Res.* 39: 193-198. (Cited in EPA, 1984).

Furst A. 1978. Tumorigenic Effects of Organomanganese Compounds on F344 Rats and Albino Mice: Brief Communications. *J. Natl. Cancer Inst.* 60: 1171-1173. (Cited in EPA, 1984).

ICF, Clement Associates. 1985. *Chemical, Physical, and Biological Properties of Compounds present at Hazardous Waste Sites.*

Kawamura, R., H. Ikuta, S. Fukuzumi, et al. 1941. Intoxication by Manganese in Well Water. Kitasato, *Arch. Exp. Med.* 18: 145-169. (Cited in EPA, 1984).

Mandzgaladze, R.N. 1967. Some Clinical and Experimental Data on the Effects of Manganese Compounds on Sexual Function. *Vopr. Gig. Tr. Prof.* 11: 126-130. (Cited in EPA, 1984).

NRC (National Research Council). 1989. *Recommended Dietary Allowances, 10th ed.* Food and Nutrition Board. National Research Council National Academy Press, Wash., D.C. p. 230-255. (Cited in HEAST).

Penalver, R. 1955. Manganese Poisoning; the 1955 Ramazzani Orations. *Med. Surg.* 24: 1-7. (Cited in EPA, 1984)

Sittig, M. 1991. *Handbook of Toxic and Hazardous Chemicals.*

U.S. EPA. *Drinking Water Regulations and Health Advisories.*

U.S. EPA. 1984. *Health Effects Assessment for Manganese and Compounds*, EPA 540/1-86/057.

U.S. EPA. *Health Effects Assessment Summary Tables (HEAST).*

U.S. EPA. *Integrated Risk Information System (IRIS).*

U.S. EPA, OERR. *CERCLA Compliance With Other Laws Manual Interim Final.* August, 1988.

U.S. EPA. 1986. *Quality Criteria for Water.* EPA 440/5-86-001.

WHO (World Health Organization). 1973. *Trace elements in human nutrition: Manganese.* Report of a WHO Expert Committee. Technical Report Service, 532, WHO, Geneva, Switzerland p. 34-36. (Cited in IRIS).

NICKEL

Use

Elemental nickel is used in electroplating, casting, batteries, and coinage. It is used in the manufacture of acid-resisting alloys, magnetic tapes, surgical, and dental instruments and colored ceramics and glass (Sittig, 1991). Elemental nickels most common use is as an alloy in the production of stainless steel because of its excellent corrosion resistant properties.

Nickel carbonyl, a common nickel compound, is formed in the extraction of pure nickel from ore.

Chemical and Physical Properties

AW: 58.71		BP: 2,732°C
SG: 8.90 at 25°C		MP: 1,453°C
Sol. (water): insoluble	VP:	1 mm Hg at 1,810°C
Sol. (organics): variable		

Fate and Transport

Nickel is most often released to the atmosphere as dusts and fumes from smelting and processing facilities, coal burning, and diesel oil combustion (EPA, 1985). The principal removal pathways of nickel from the atmosphere are wet and dry deposition. Chemical interactions of nickel in the atmosphere generally result in elemental nickels conversion to nickel oxide (EPA, 1984).

In aquatic environments, nickel generally exists in solution as hydroxide, carbonate, sulfate, and organic complexes. The environmental fate of nickel in aquatic media appears to be dependent on the extent of pollution. In highly polluted waters, nickel is more apt to remain dissolved (EPA, 1984).

In soils, the amount of organic matter, iron oxides, and manganese oxides, may determine the fate of nickel. In soils with high iron and manganese oxide content, nickel would sorb and remain stable but, in soils with high organic content, nickel would complex and become more mobile (EPA, 1984).

Pharmacokinetics

Nickel is absorbed by humans and animals through ingestion, inhalation and, to a lesser extent, percutaneous exposure. Horak and Sunderman (1973) reported that, of the 160 to 500 µg nickel ingested daily by the average man, 1 to 10 percent is absorbed.

Absorbed nickel appears to be distributed throughout the pancreas, testes, and bones in calves and throughout the kidneys, liver, heart, and testes in rats (EPA, 1985). Nickel is transported through the body's sera primarily by serum albumin in man, rabbits, rats, and bovine (EPA,

1985). In man, it is excreted in the urine and is deposited in hair follicles. Ingested metal that is not absorbed is excreted in the feces (EPA, 1985).

Human Toxicity

Noncarcinogenic Effects

Systemic Effects

Ambrose et al. (1976) exposed rats to nickel sulfate hexahydrate in concentrations of 0, 100, 1000, or 2500 ppm as Nickel in the diet for 2 years. High-dose rats exhibited decreased body weights, increased heart-to-body weight ratios and decreased liver-to-body weight ratios. Inhalation studies indicate that chronic exposure to high concentrations of nickel fumes can cause severe toxic effects, including pathological respiratory changes and death in humans. Less severe effects, including dermatitis, sinusitis, and nasal mucosal injury have been reported by workers occupationally exposed to various nickel compounds (ICF, 1985).

Teratogenic and Other Developmental Effects

Inhalation of nickel carbonyl vapors by dams caused a highly significant increase in eye malformation in newborns. The teratogenic effects of nickel carbonyl were found to be dose related (EPA, 1984).

Mutagenic Effects

Nickel carbonyl has been found to bind to liver and kidney DNA (Hui and Sunderman, 1980). Numerous studies cited in IRIS reveal that nickel subsulfide induces morphologic transformation in Syrian hamster embryos, and baby hamster kidney (BHK-21) cell cultures, sister chromatid exchange in human lymphocytes, and DNA strand breaks. As cited in IRIS, Sunderman (1984) observed nickel subsulfide to concentrate in the cell nucleus in *in vitro* assays.

Carcinogenic Effects

There have been numerous case studies performed on nickel smelting workers indicating that exposure to nickel fumes increases the chance of lung and nasal cavity tumors. Pedersen, et al. (1973) and Doll, et al. (1977) reported that nickel refinery workers exposed to 20 to 26 mg Ni/m^3 on a chronic basis developed a significantly higher number of tumors than would be expected in a normal population. In Pedersen's studies, the risk of lung cancer increased 3.75 fold and the risk of nasal cancer increased 27 fold. More recent refinery methods and more stringent occupational exposure regulations have greatly reduced the carcinogenic potential to workers.

There is not sufficient evidence concerning oral exposure to nickel to draw any conclusions.

Nickel subsulfide, nickel carbonyl, nickel oxides, and nickel sulfate are all thought to indure tumors in laboratory animals (ICF, 1985).

Ecotoxicity

Nickel tends to be more toxic to aquatic life when there are lower concentrations of iron and manganese in the water (decreased hardness). Nickel salt concentrations between 510 and 46,200 µg/L were determined to be acutely toxic to freshwater species (ICF, 1985). Saltwater algae have shown stunted growth in nickel concentrations as low as 1,000 µg/L.

Standards, Criteria and Guidelines

EPA Class A Carcinogen (refinery dust, subsulfide)
EPA Class B2 Carcinogen (carbonyl)

Oral Slope Factor:	NA	
Chronic Oral RfD:	2.0×10^{-2} mg/kg/day (soluble salts)	
Subchronic Oral RfD:	2.0×10^{-2} mg/kg/day (soluble salts)	
MCL:	0.1 mg/l	
AWQC:	Acute:	1400 µg/L
	Chronic:	160 µg/L (hardness dependent)

BIBLIOGRAPHY

Ambrose, A.M., et al. 1976. Long-term to toxicologic assessment of nickel in rats and dogs. *J. Food Sci. technol.* 13:181-187. (cited in IRIS).

Colborne, Roberts, et al. 1983. (full reference not given in IRIS).

Doll, R., J.D. Mathews and L.G. Morgan. 1977. Cancers of the Long and Nasal Sinuses in Nickel Workers: A Reassessment of the Period of Risk. *Br. J. Ind. Med.* 34: 102-105. (Cited in EPA, 1985).

Gilman, J.P.W. .and G.M. Ruckerbauer. 1962. Metal carcinogenisis. I. Observations on the carcinogenicity of a refinery dust, cobalt oxide, and colloidal thorium dioxide. *Cancer Res.* 22: 152-157. (cited in IRIS).

Horak, E. and F. W. Sunderman, Jr. 1973. Fecal Nickel Excretion by Healthy Adults. *Clin. Chem.* 19: 429-430. (Cited in EPA, 1985).

Hui, G. and F.W. Sunderman. 1980. Effects of nickel compounds on incorporation of thymidine-34 into DNA in rat liver and kidney. *Carcinogenesis.* 1:297-304. (Cited in IRIS).

ICF, Clement Associates. 1985. *Chemical, Physical and Biological Properties of Compounds Present at Hazardous Waste Sites.*

Pederson, E., A. Andersen and H. Hogetveit. 1973. Cancer of Respiratory Organs Among Workers at a Nickel Refinery in Norway. *Int. J. Cancer.* 12: 32-41. (Cited in EPA, 1985).

Sittig, M. 1991. *Handbook of Toxic and Hazardous Chemicals.*

U.S. EPA. *Drinking Water Regulations and Health Advisories.*

U.S. EPA. *Health Advisory for Nickel, Office of Drinking Water.*

U.S. EPA. *Health Effects Assessment for Nickel.* EPA 540/1-86/018.

U.S. EPA. *Health Effects Assessment Summary Tables (HEAST).*

U.S. EPA. *Integrated Risk Information System (IRIS).*

U.S. EPA, OERR. *CERCLA Compliance With Other Laws Manual Interim Final.* August, 1988.

U.S. EPA. 1986. *Quality Criteria for Water.* 2 EPA 440/5-86-001.

THALLIUM

Use

Thallium and its compounds are used as catalysts in certain organic reactions, in phosphor activators, in bromoiodide crystals for lenses, plates, and prisms in infrared optical instruments, in photoelectric cells, in mineralogical analysis; in alloys with mercury in low-temperature thermometers, switches and closures; in high-density liquids, dyes and pigments; and in the manufacture of optical lenses, fireworks, and imitation precious jewelry. It forms a stainless alloy with silver and a corrosion resistant alloy with lead. Its medicinal use for epilation is almost discontinued (Sittig, 1991). Prior to 1972, thallium and its compounds were used as rodenticides, fungicides, and insecticides (Sittig, 1991; Stokinger, 1981).

Physical and Chemical Properties

AW:	204.37	MP:	303.5°C
SG:	11.85 g/mc^3	BP:	1457°C
VP:	10 mm Hg at 1000°C		
Sol. (water):	insoluble		

Fate and Transport

Cement factories, coal burning power plants, and metal smelters are the principal sources of thallium in the environment (Sharma et al., 1986; Brockhaus et al., 1980, 1981). Atmospherically, thallium may be present in its elemental form, as oxides of Tl, as Tl_2S, or Tl_2So_4. Tl_2S is likely to be speciated to Tl_2SO_4 and Tl_2O will be rapidly hydrolyzed to TlOH by the moisture in the atmosphere (U.S. EPA, 1988).

Both TlOH and Tl_2SO_4 are most likely removed from the atmosphere by wet deposition given their water solubilities. Tl_2O_3, however, may persist in the atmosphere longer because it is insoluble in water and, therefore, will be removed by dry deposition (U.S. EPA, 1988).

In aquatic systems, insoluble forms of thallium will accumulate in the sediment (Mathis and Kevern, 1975). Kempton et al. (1987a,b) reports that thallium may be removed from the water by sorption onto suspended solids in water. Most of the soluble thallium that enters aquatic systems will remain in the soluble state due to its formation of soluble complexes with inorganic and organic ligands (Stephenson and Lester, 1987a,b). These complexes are even more stable at higher pHs (O'Shea and Mancy, 1978). Wallwork-Barber et al. 91985) report that thallium in water may be transported to fish and vegetation. The bioconcentration factor of thallium in whole aquatic organisms ranges from 12-34 (Zitko and Carson, 1975; Barrows et al., 1980).

In soils, leaching of thallium, particularly from sandy soils, appears to be likely given its transport in water (U.S. EPA, 1988). Cataldo and Wildung (1983) report that up to 10 percent of the thallium absorbed in plant roots from soil may be transported from the root to the shoot of the plant.

Pharmacokinetics

U.S. EPA (1988) reports that numerous studies reveal that absorption of soluble thallium by any route of exposure is rapid and virtually complete, although dermal absorption is not likely to be significant in environmental exposure. Several studies indicate that distribution of thallium from the blood is rapid and widespread; with highest levels detected in the kidney, heart, and liver; and lowest levels detected in the nervous system and body fat. Lie et al. (1960) reports that the relative concentrations in different tissues appear to be independent of the route of administration and the time after administration. In addition, Sabbioni et al. (1980) and Gregus and Klaasen (1986) found no correlation between tissue concentrations and the valance of thallium administered or the dosage, respectively. The U.S. EPA (1988) reports that several studies indicate that thallium translocates to the placenta and fetus, but levels in the fetus are substantially lower than those in maternal tissues. Sabbioni et al. (1980) hypothesizes that thallium *in vivo* is transformed to one oxidation state. Barclay et al. (1953) and Richelmi et al. (1980) report that, in humans, excretion of thallium occurs predominantly in the urine. A range of estimated excretion half-lives have been reported with Talas et al. (1983) reporting 2.15 days for tracer doses in ambulatory heart patients and Barclay et al. (1953) and U.S. EPA (1980) reporting 21.7 days in a terminal cancer patient.

Human Toxicity

Noncarcinogenic Effects

Systemic Effects

U.S. EPA (1988) reports that thallium salts are potent poisons that cause acute toxicity in humans. Accidental ingestion of thallium salt rodenticides and insecticides, internal and topical use of thallium as a depilatory agent have all resulted in human poisoning (Gettler and Weiss, 1943; Moeschlin, 1980). In children, Bedford (1928) reports that acute toxicity appears to be approximately 6 mg thallium/kg/day. Moeschlin (1980) reports approximately 8-12 mg thallium/kg as the average lethal dose for adults. Independent of the species or the type of thallium salt administered, U.S. EPA (1988) reports that the acute oral LD_{50} values in rats and mice range from 16 to 35 mg thallium/kg.

Chronic oral exposure of a population living in the vicinity of a cement factory that discharged large quantities of thallium into the atmosphere through the ingestion of fruits and vegetables grown in the area appears to have resulted in an increased incidence of neurological and subjective symptoms (Brockhaus et al., 1980, 1981; Dolgner et al., 1983). Subchronic oral exposure of laboratory animals to concentrations greater than 0.25 mg/kg/day resulted in neurological and skeletal muscle effects (Mazo et al., 1983, Deshimaru et al., 1977), hair loss, elevated kidney weights, body weight loss, and mortality (Downs et al., 1960).

U.S. EPA (1979) exposed rats intermittently to thallium (III) oxide via inhalation at 0.5 - 2.0 mg/m_3. Deteriorating health and increased mortality were observed. However, no adverse health effects were observed in workers occupationally exposed to thallium in a magnesium seawater battery plant (Marcus, 1985) or in cement production (Schaller et al., 1980); Ludolph et al., 1986).

Teratogenic and Other Developmental Effects

U.S. EPA (1988) reports on numerous studies which indicate that thallium results in achondroplastic malformations when injected into developing chicken eggs, or tested in mammalian whole embryo cultures or limb bud cultures. Gibson and Becker (1970) observed reduced fetal body weight, hydronephrosis, and the absence of vertebral bodies following parenteral administration of greater than 2 mg thallium/kg/day to pregnant rats. A slight increase in fetal loss was observed following oral administration of thallium to rats (≥2 mg/kg/day) and mice (≥ 4 mg/kg/day) (Roll and Matthiaschk, 1981). Reduced survival at weaning in both species and reduced growth rate in mice were observed in the offspring of rats and mice allowed to deliver, as well. Bornhausen and Hagen (1984) report that adult offspring of dams treated with thallium during gestation had significant learning deficits in a lever-pressing behavior conditioning test.

U.S. EPA (1988) reports that adult male rats exposed to 0.74 mg thallium/kg/day in the drinking water had decreased sperm motility, inhibition of ß-glucoronidase activity, and histopathological alterations of the testes after 60 days of exposure but not after 30 days.

Mutagenic Effects

Data on the mutagenicity of thallium is mixed. Negative results have been obtained in reverse mutation tests (Kanematsu et al., 1980; Singh, 1983) and in tests for effects on cell division (Loveless et al., 1954). Positive results were obtained in a rec assay (Kanematsu et al., 1980) and in several mammalian test systems, including a dominant lethal test in male rats (Zasukhina et al., 1983).

Carcinogenic Effects

Data regarding the carcinogenicity of thallium were not available in the literature reviewed.

Ecotoxicity

In freshwater aquatic systems, U.S. EPA (1980) reports that acute sensitivity of *Daphnia magna* and the fathead minnow to thallium were similar, with LC_{50} values in the range of 910 to 2180 µg/l. LC_{50} values for the bluegill were approximately two

orders of magnitude higher. *Daphnia magna* and the fathead minnow also had similar chronic values; 130 and 57 µg Tl/l, respectively. Exposure of an alga to 110 and 100 µg Tl/l resulted in a 50 percent reduction in chlorophyll *a* and cell numbers, respectively. Atlantic salmon had the highest bioconcentration factor for fishes with a value of 130 for muscle tissue. This species appears to be particularly sensitive to thallium; concentrations as low as 20 µg/l resulted in partial mortality after about 100 days exposure.

In saltwater systems, the mysid shrimp had the greatest acute sensitivity with an LC_{50} of 2130 µg thallium/l. The sheepshead minnow and tidewater silverside had exhibited similar sensitivity to thallium with 96-hour LC_{50} values of 20,900 µg/l and 24,000 µg/l, respectively. 8,400 µg/l produced chronic effects in the sheepshead minnow. 4,080 µg/l resulted in a 50 percent reduction in photosynthesis in a saltwater algal species. Bioconcentration factors less than 20 were observed in two bivalve species exposed for 40 to 88 days.

No data on the ecotoxicity of thallium in terrestrial systems were available in the literature reviewed.

Standards, Criteria and Guidelines

Unclassified by EPA as to carcinogenicity

Oral Slope Factor:	NA
Chronic Oral RfD:	7.0×10^{-5} mg/kg/day (thallic oxide value)
Subchronic Oral RfD:	7.0×10^{-4} mg/kg/day
MCL	2 µg/L
AWQC:	Acute: 1400 µg/L (LOEL)
	Chronic: 40 µg/L (LOEL)

BIBLIOGRAPHY

Barclay, R.K., et al. 1953. Distribution and excretion of radioactive thallium in the chick embryo, rat and man. *J. Pharmacol. Exp. Ther.* 107: 178-187. (cited in HEED).

Barrows, M.E., et al. 1980. Bioconcentration and elimination of selected water pollutants by blue gill sunfish (*Lepomis macrochirus*). In: *Symp. Dyn. Exposure Hazard Assess. Toxic Chem.*, 1978. Ann Arbor Science, Ann Arbor, MI, p. 379-392. (cited in HEED).

Bornhausen, M. and U. Hagen. 1984. Operant behavior performance changes in rats after prenatal and postnatal exposure to heavy metals. *IRCS Med. Sci.* 12: 805-806. (cited in HEED).

Brockhaus, A., et al. 1980. Excessive thallium absorption among a population living near a thallium emitting cement plant. In: *Mechanisms of Toxicity and Hazard Evaluation.* B. Holmstedt, R. Lauwerys, M. Mercier and M. Roberfroid, Ed. Elsevier/North-Holland Biomedical Press, The Netherlands. p. 565-568. (cited in HEED).

Brockhaus, A., et al. 1981. Intake and health effects of thallium among a population living in the vicinity of a cement plant emitting thallium containing dust. *Int. Arch. Occup. Environ. Health.* 48: 375-389. (cited in HEED).

Cataldo, D. and R. Wildung. 1983. The role of soil and plant metabolic processes in controlling trace element behavior and bioavailability to animals. *Sci. Total Environ.* 28: 159-168. (cited in HEED).

Deshimaru, M., et al. 1977. Electron microscopic study of experimental thallotoxicosis. *Folia Psych. Neurol. Jpn.* 31: 269-275. (cited in HEED).

Dolgner, R., et al. 1983. Repeated surveillance of exposure to thallium in a population living in the vicinity of a cement plant emitting dust containing thallium. *Int. Arch. Occup. Environ. Health.* 52: 79-94. (cited in HEED).

Downs, W.L., et al. 1960. Acute and subacute toxicity studies of thallium compounds. *Am. Ind. Hyg. Assoc.* 21: 399-406. (cited in HEED).

Gettler, A.O. and L. Weiss. 1943. Thallium poisoning. III. Clinical toxicology of thallium. *Am. J. Clin. Pathol.* 13: 422-429. (cited in HEED).

Gibson, J.E. and B.A. Becker. 1970. Placental transfer, embrytoxicity and teratogenicity of thallium sulfate in normal and potassium-deficient rats. *Toxicol. Appl. Pharmacol.* 16: 120-132. (cited in HEED).

Gregus, Z. and C.D. Klaassen. 1986. Disposition of metals in rats: A comparative study of fecal, urinary and biliary excretion and tissue distribution of eighteen metals. *Toxicol. Appl. Pharmacol.* 85: 24-38. (cited in HEED).

Kanematsu, N., et al. 1980. Rec assay and mutagenicity studies on metal compounds. 77: 109-116. (cited in HEED).

Kempton, S., et al. 1987a. Heavy metal removal in primary sedimentation. I. The influence of metal solubility. *Sci. Total Environ.* 63: 247-258. (cited in HEED).

Kempton, S., et al. 1987b. Heavy metal removal in primary sedimentation. II. The influence of metal speciation and particle size distribution. *Sci. Total Environ.* 63: 231-246. (cited in HEED).

Lie, R., et al. 1960. The distribution and excretion of thallium-204 in the rat with suggested MPC's and a bioassay procedure. *Health Phys.* 2: 334-340. (cited in HEED).

Loveless, L.E., et al. 1954. Survey of effects of chemical on division and growth of yeast and *Escherichia coli. J. Bacteriol.* 68: 637-644. (cited in HEED).

Ludolph, A., et al. 1986. Chronic thallium exposure in cement plant workers: Clinical and electrophysiological data. *Trace Elem. Med.* 3(3): 121-125. (cited in HEED).

Manzo, L., et al. 1983. *Environmental toxicology research on thallium: Metabolic and toxicological studies in the rat as carried out by nuclear and radioanalytical methods.* NTIS PB 83-133249. (cited in HEED).

Mathis, B.J. and N.R. Kevern. 1975. Distribution of mercury, cadmium, lead, and thallium in a eutrophic lake. *Hydrobiologia.* 46(2-3): 207-222. (cited in HEED).

MRI (Midwest Research Institute). 1986. *Subchronic (90-day) toxicity study of thallium sulfate in Sprague-Dawley rats.* Office of Solid Waste, U.S. EPA, Wash., D.C. (cited in HEAST).

Moeschlin, S. 1980. Thallium poisoning. *Clin. Toxicol.* 17: 133-146. (cited in HEED).

O'Shea, T.A. and K.H. Mancy. 1978. The effect of pH and hardness of metal ions on the competitive interaction between trace metal ions and inorganic and organic complexing agents found in natural waters. *Water Res.* 12(9): 703-711. 1978 (cited in HEED).

Richelmi, P., et al. 1980. Salivary levels of thallium in acute human poisoning. *Arch. Toxicol.* 43: 321-325. (cited in HEED).

Roll, R. and G. Matthiaschk. 1981. Investigations on embryotoxic effects of thallium chloride and thallium acetate in mice and rats. *Teratology.* 24(2): 46A-47A. (cited in HEED).

Sabbioni, E., et al. 1980. Metabolic fate of different inorganic and organic species of thallium in the rat. *Sci. Total Environ.* 15(2): 123-135. (cited in HEED).

Schaller, K.H., et al. 1980. Investigations of thallim-exposed workers in cement factories. *Int. Arch. Occup. Environ. Health.* 47(3): 223-321. (cited in HEED).

Sharma, J., et al. 1986. Hazards and analysis of thallium - A review. *Toxicol. Environ. Chem.* 11: 93-116. (cited in HEED).

Singh, I. 1983. Induction of reverse mutation and mitotic gene conversion by some metal compounds in *Saccharomyces cerevisiae. Mutat. Res.* 117: 149-152. (cited in HEED).

Sittig, M. 1991. *Handbook of Toxic and Hazardous Chemicals.*

Stephenson, T. and J.N. Lester. 1987a. Heavy metal behavior during the activated sludge process. I. Extent of soluble and insoluble metal removal. *Sci. Total Environ.* 63: 199-214. (cited in HEED).

Stephenson, T. and J.N. Lester. 1987b. Heavy metal behavior during the activated sludge process. II. Insoluble metal removal mechanisms. *Sci. Total Environ.* 63: 215-231. (cited in HEED).

Stokinger, H.E. 1981. The metals: 32 thallium, TI. In: *Patty's Industrial Hygiene and Toxicology, Vol. 2A, 3rd Ed.*, G.C. Clayton and F.E. Clayton, Ed. John Wiley and Sons, Inc., New York. p. 1914-1931. (cited in HEED).

Talas, A. and H.H. Wellhoener. 1983. Dose-dependency of thallium (1+) kinetics as studied in rabbits. *Arch. Toxicol.* 53(1): 9-16. (cited in HEED).

U.S. EPA. 1979. Study of Carcinogenicity and Toxicity of Inhaled Antimony Trioxide, Antimony Ore Concentration and Thallic Oxide in Rats. MRI Project No. 4466-B. Contract No. 210-77-0156. OTS Fiche No. 0511065. (cited in HEED).

U.S. EPA. 1980. *Ambient Water Quality Criteria Document for Thallium.*

U.S. EPA. 1988. *Health and Environmental Effects Document (HEED).*

U.S. EPA. *Health Effects Assessment Summary Tables (HEAST).*

U.S. EPA. *Drinking Water Regulations and Health Advisories.*

U.S. EPA, OERR. *CERCLA Compliance With Other Laws Manual Interim Final.* August, 1988.

U.S. EPA. 1986. *Quality Criteria for Water.* EPA 440/5-86-001.

Wallwork-Barber, M.K., et al. 1985. Thallium movement in a simple aquatic ecosystem. *J. Environ. Sci. Health, Part A.* 20: 689-700. (cited in HEED).

Zasukhina, G.D., et al. 1983. Mutagenic effect of thallium and mercury salts on rodent cells with different repair activities. *Mutat. Res.* 124(2): 163-173. (cited in HEED).

Zitko, V. and W.V. Carson. 1975. Accumulation of thallium in clams and mussels. *Bull. Environ. Contam. Toxicol.* 14(5): 530-533. (cited in HEED).

VANADIUM

Use

Vanadium pentoxide is used as a catalyst in the production of several industrial chemicals. It is also used as a photographic developer, as a coating for welding electrodes, and as an alloying agent (ACGIH, 1984).

Chemical and Physical Properties

AW: 50.9
SG: 5.96 at 20°C
Sol. (water): at 20°C insoluble
Sol. (organics): insoluble

BP: 3,380°C
MP: 1,890°C

Fate and Transport

The environmental fate of vanadium varies with each compound. Some compounds are volatile so, atmospheric transport would be a legitimate fate process (ICF, 1985). Vanadium appears to become more water soluble in acidic soils, thus becoming more leachable, and is known to bioaccumulate slightly.

Pharmacokinetics

Vanadium is thought to be stored primarily in fat and blood serum but has been detected in the lungs and intestines in humans (U.S. HEW, 1969).

Human Toxicity

Noncarcinogenic Effects

Systemic Effects

The principle systemic effects of chronic exposure to vanadium are the irritation of the skin and eyes. Oral exposure to vanadium is known to cause gastrointestinal disturbances. Inhalation exposure to vanadium is known to cause irritation of the lungs and after repeated exposures difficulty in breathing and bronchitis are known to occur (NIOSH, 1977). Vanadium's toxicity seems to increase with the increase in valence number (ICF, 1985).

Teratogenic and Other Developmental Effects/Mutagenic Effects

Vanadium and its compounds have not displayed mutagenic, teratogenic, or developmental effects in several studies performed on laboratory animals (ICF, 1985).

Carcinogenic Effects

Vanadium is not classified as to human carcinogenicity because of insufficient human or animal data. In one study, researchers exposed Swiss mice to vanadyl sulfate at concentrations of 19.8 mg/kg bw for their lifetime. There was no evidence that vanadyl sulfate caused tumors in the mice (NIOSH, 1977). Numerous other studies have resulted with similar conclusions (NIOSH, 1977).

Ecotoxicity

Freshwater organisms have LC_{50} values ranging between 5,000 and 100,000 µg/L. The average LC_{50} value for freshwater organisms is around 10,000 µg/L (ICF, 1985).

No further data regarding the ecotoxicity to wildlife were located.

Standards, Criteria and Guidelines

EPA Class D Carcinogen

Oral Slope Factor:	NA
Chronic Oral RfD:	7.0×10^{-3} mg/kg/day
Subchronic Oral RfD:	7.0×10^{-3} mg/kg/day
MCL:	NA

BIBLIOGRAPHY

American Conference of Governmental Industrial Hygienists. 1984. *Documentation of the Threshold Limitation Values.*

ICF, Clement Associates. 1985. *Chemical, Physical and Biological Properties of Compounds Present at Hazardous Waste Sites.*

NIOSH. 1977. *Criteria for a Recommended Standard for The Occupational Exposure to Vanadium.*
Schroeder, J.A., et al. 1970. Zirconium, niobium, antium, antimony, Vanadium, and lead in rats: Life-term studies. *J. Nutr.* 100(1): 59-68. (cited as principal oral RfD study in HEAST).

Sittig, M. 1991. *Handbook of Toxic and Hazardous Chemicals.*

U.S. Dept. of Health, Education and Welfare (U.S. HEW). 1969. *Preliminary Air Pollution Survey of Vanadium and Its Compounds.*

U.S. EPA. *Drinking Water Regulations and Health Advisories.*

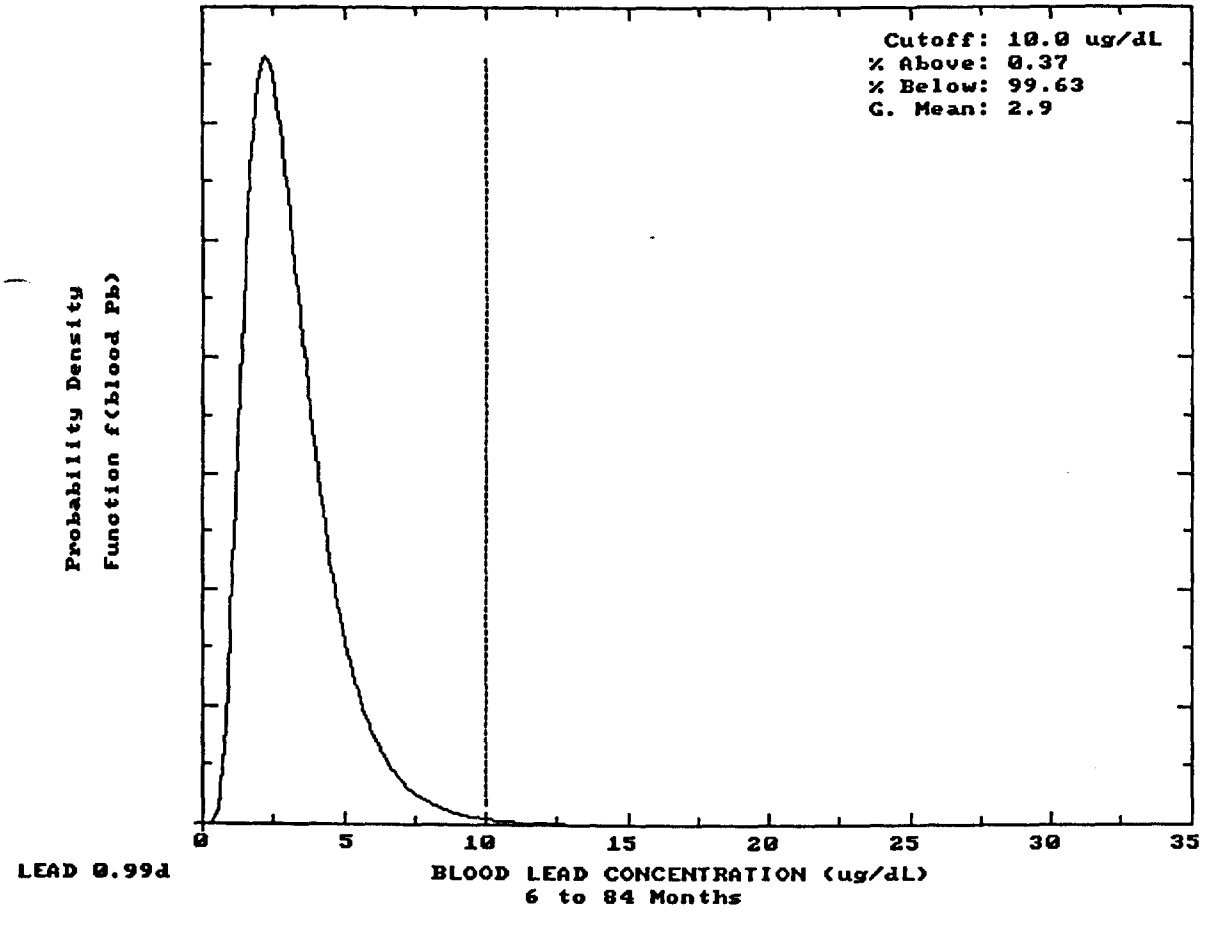
U.S. EPA. *Health Effects Assessment Summary Tables (HEAST).*

U.S. EPA, OERR. *CERCLA Compliance With Other Laws Manual Interim Final.* August, 1988.

APPENDIX D

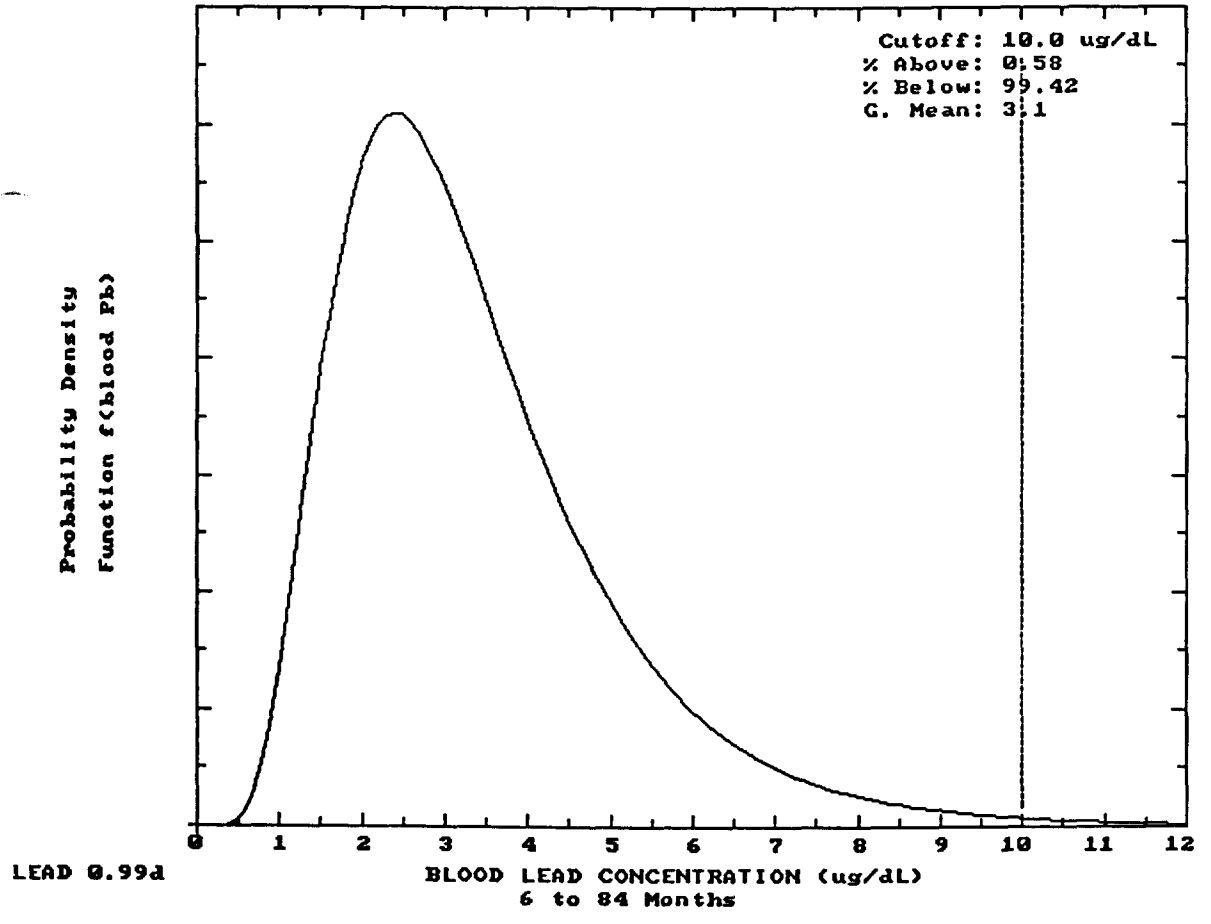
LEAD INTEGRATED EXPOSURE UPTAKE BIOKINETIC (IEUBK) MODEL RESULTS

Figure 1. Illustrated distribution of blood lead concentrations that result from children ingesting the average lead concentrations detected in ground water and surface soils at the Burgess Brothers Superfund site. The distribution, calculated by the EPA Uptake Biokinetic model for lead, predicts that ingesting the average lead concentrations in ground water (1.17 µg/l) and surface soil (79.6 mg/kg) will result in blood lead concentrations in excess of 10 micrograms per deciliter for 0.37 percent of children ages 0.5 to 7 years. EPA's goal is to maintain the blood lead of 95% of children below 10 µg/dL.



L95-651.apa

Figure 2. Illustrated distribution of blood lead concentrations that result from children ingesting the average lead concentrations detected in surface soils at the Burgess Brothers Superfund site. The distribution, calculated by the EPA Uptake Biokinetic model for lead, predicts that ingesting the average lead concentrations in surface soils (79.6 mg/kg) and assuming a default concentration of 4.0 ug/L lead in groundwater will result in blood lead concentrations in excess of 10 micrograms per deciliter for 0.58 percent of children ages 0.5 to 7 years. This scenario meets EPA's goal to maintain blood levels of 95% of children below 10 µg/dL.



L95-651.apa

APPENDIX E

ECOLOGICAL RISK TABLES

TABLE E-1. PLANT CONCENTRATIONS OF COCS, WETLAND SOILS.

Contaminant of Concern	Soil Concentration		Log Kow[1]	Plant Uptake Factor[2]	Plant Concentration[3]	
	Mean (mg/kg)	Maximum (mg/kg)			Mean (mg/kg)	Maximum (mg/kg)
Acetone	1.28E-01	1.10E+00	-0.24	1.47E-01	1.88E-03	1.62E-02
Benzene	6.05E-03	2.00E-02	2.12	7.48E-01	4.52E-04	1.50E-03
2-Butanone	4.66E-02	3.90E-01	0.26	3.04E-01	1.42E-03	1.19E-02
Carbon Disulfide	8.85E-03	3.70E-02	2.00	7.69E-01	6.81E-04	2.85E-03
1,1-Dichloroethane	6.05E-03	2.00E-02	1.79	7.84E-01	4.74E-04	1.57E-03
1,1-Dichloroethene	7.92E-03	4.80E-02	1.84	7.81E-01	6.18E-04	3.75E-03
1,2-Dichloroethene (Total)	4.52E+00	6.60E+01	0.70	4.86E-01	2.20E-01	3.21E+00
Ethyl Benzene	2.13E-02	2.30E-01	3.15	3.63E-01	7.73E-04	8.35E-03
4-Methyl-2-Pentanone	1.41E-02	6.80E-02	1.19	5.64E-01	7.92E-04	3.84E-03
Tetrachloroethene	4.24E-01	5.30E+00	2.60	5.95E-01	2.52E-02	3.15E-01
Toluene	1.12E+00	1.50E+01	2.73	5.42E-01	6.09E-02	8.13E-01
1,1,1-Trichloroethane	6.12E-03	2.10E-02	2.50	4.81E-01	2.94E-04	1.01E-03
Trichloroethene	1.38E-01	1.50E+00	2.38	6.76E-01	9.35E-03	1.01E-01
Vinyl Chloride	3.37E-01	4.90E+00	1.38	6.74E-01	2.27E-02	3.30E-01
Xylenes, Total	6.72E-02	8.40E-01	3.26	3.19E-01	2.14E-03	2.68E-02
Acenaphthylene	4.41E-01	9.10E-01	3.70	1.73E-01	7.63E-03	1.57E-02
Anthracene	5.89E-01	1.50E+00	4.45	4.22E-02	2.48E-03	6.33E-03
Benzo(a)anthracene	1.44E+00	4.90E+00	5.60	1.98E-03	2.85E-04	9.70E-04
Benzo(a)pyrene	1.36E+00	4.60E+00	6.06	4.30E-04	5.86E-05	1.98E-04
Benzo(b)fluoranthene	1.89E+00	6.70E+00	6.06	4.30E-04	8.12E-05	2.88E-04
Benzo(k)fluoranthene	1.44E+00	4.90E+00	6.06	4.30E-04	6.19E-05	2.11E-04
Chrysene	1.74E+00	6.10E+00	5.61	1.92E-03	3.34E-04	1.17E-03
Fluoranthene	3.21E+00	1.20E+01	4.90	1.45E-02	4.66E-03	1.74E-02
Indeno(1,2,3-cd)pyrene	1.04E+00	3.30E+00	6.50	8.49E-05	8.82E-06	2.80E-05
Phenanthrene	3.71E+00	1.40E+01	4.46	4.13E-02	1.53E-02	5.78E-02
Pyrene	3.21E+00	1.20E+01	4.88	1.53E-02	4.92E-03	1.84E-02
Aluminum	8.99E+03	2.45E+04	NA	4.00E-03	3.60E+00	9.80E+00
Antimony	7.88E-01	5.50E+00	NA	2.00E-01	1.58E-02	1.10E-01
Arsenic	2.39E+00	4.20E+00	NA	4.00E-02	9.56E-03	1.68E-02
Barium	7.56E+01	2.80E+02	NA	1.50E-01	1.13E+00	4.20E+00
Beryllium	3.81E-01	1.30E+00	NA	1.00E-02	3.81E-04	1.30E-03
Cadmium	3.78E-01	2.39E+00	NA	5.50E-01	2.08E-02	1.31E-01
Chromium	8.57E+00	1.98E+01	NA	7.50E-03	6.43E-03	1.49E-02
Cobalt	4.84E+00	1.70E+01	NA	2.00E-02	9.68E-03	3.40E-02
Copper	1.22E+01	5.10E+01	NA	4.00E-01	4.86E-01	2.04E+00
Cyanide	6.36E-01	1.90E+00	NA	--	0.00E+00	0.00E+00
Iron	1.34E+04	2.94E+04	NA	4.00E-03	5.37E+00	1.18E+01
Lead	1.22E+02	1.04E+03	NA	4.50E-02	5.51E-01	4.68E+00
Manganese	2.54E+02	1.22E+03	NA	2.50E-01	6.36E+00	3.05E+01
Mercury	1.25E-01	3.60E-01	NA	9.00E-01	1.13E-02	3.24E-02
Nickel	9.77E+01	5.96E+02	NA	6.00E-02	5.86E-01	3.58E+00

TABLE E-1. PLANT CONCENTRATIONS OF COCS, WETLAND SOILS (cont...)

Contaminant of Concern	Soil Concentration			Plant	Plant Concentration[3]	
	Mean (mg/kg)	Maximum (mg/kg)	Log Kow[1]	Uptake Factor[2]	Mean (mg/kg)	Maximum (mg/kg)
Selenium	2.84E-01	5.20E-01	NA	2.50E-02	7.10E-04	1.30E-03
Thallium	1.28E-01	2.40E-01	NA	4.00E-03	5.12E-05	9.60E-05
Vanadium	1.37E+01	2.52E+01	NA	5.50E-03	7.56E-03	1.39E-02
Zinc	1.09E+02	5.06E+02	NA	1.50E+00	1.64E+01	7.59E+01

NA: Not Applicable

[1] from Superfund Public Health Evaluation Manual, 1986.

[2] Organics from Briggs et al. (1982), Inorganics from Baes et al. (1984).

[3] Plant concentration = Soil concentration x Plant uptake factor.

Note: Plant concentration converted from dry weight to wet weight by multiplying by 0.1 (Baes et al., 1984).

TABLE E-2. EARTHWORM CONCENTRATIONS OF COCS, WETLAND SOILS.

Contaminant of Concern	Soil Concentration		Earthworm	Earthworm Concentration[2]	
	Mean (mg/kg)	Maximum (mg/kg)	Bioaccumulation Factor[1]	Mean (mg/kg)	Maximum (mg/kg)
Acetone	2.64E-01	1.10E+00	1.54E+00 a	1.02E-01	4.24E-01
Benzene	8.36E-03	2.00E-02	2.40E+00 a	5.01E-03	1.20E-02
2-Butanone	9.06E-02	3.90E-01	1.69E+00 a	3.83E-02	1.65E-01
Carbon Disulfide	1.44E-02	3.70E-02	2.34E+00 a	8.40E-03	2.16E-02
1,1-Dichloroethane	8.36E-03	2.00E-02	2.25E+00 a	4.70E-03	1.13E-02
1,1-Dichloroethene	1.24E-02	4.80E-02	2.27E+00 a	7.01E-03	2.72E-02
1,2-Dichloroethene (Total)	9.68E+00	6.60E+01	1.84E+00 a	4.45E+00	3.04E+01
Ethyl Benzene	4.10E-02	2.30E-01	2.90E+00 a	2.97E-02	1.67E-01
4-Methyl-2-Pentanone	2.09E-02	6.80E-02	2.01E+00 a	1.05E-02	3.42E-02
Tetrachloroethene	8.88E-01	5.30E+00	2.62E+00 a	5.82E-01	3.47E+00
Toluene	2.40E+00	1.50E+01	2.68E+00 a	1.61E+00	1.01E+01
1,1,1-Trichloroethane	8.50E-03	2.10E-02	2.57E+00 a	5.46E-03	1.35E-02
Trichloroethene	2.86E-01	1.50E+00	2.52E+00 a	1.80E-01	9.45E-01
Vinyl Chloride	7.12E-01	4.90E+00	2.09E+00 a	3.72E-01	2.56E+00
Xylenes, Total	1.39E-01	8.40E-01	2.96E+00 a	1.03E-01	6.22E-01
Acenaphthylene	4.41E-01	9.10E-01	1.00E+00 d	1.10E-01	2.28E-01
Anthracene	5.89E-01	1.50E+00	8.30E-02 b	1.22E-02	3.11E-02
Benzo(a)anthracene	1.44E+00	4.90E+00	1.86E-01 b	6.69E-02	2.28E-01
Benzo(a)pyrene	1.36E+00	4.60E+00	6.23E-01 b	2.12E-01	7.16E-01
Benzo(b)fluoranthene	1.89E+00	6.70E+00	7.13E-01 b	3.37E-01	1.19E+00
Benzo(k)fluoranthene	1.44E+00	4.90E+00	6.23E-01 b	2.24E-01	7.63E-01
Chrysene	1.74E+00	6.10E+00	3.02E-01 b	1.31E-01	4.61E-01
Fluoranthene	3.21E+00	1.20E+01	1.47E-01 b	1.18E-01	4.41E-01
Indeno(1,2,3-cd)pyrene	1.04E+00	3.30E+00	5.29E-01 b	1.37E-01	4.36E-01
Phenanthrene	3.71E+00	1.40E+01	1.77E-01 b	1.64E-01	6.20E-01
Pyrene	3.21E+00	1.20E+01	2.76E-01 b	2.22E-01	8.28E-01
Aluminum	8.99E+03	2.45E+04	1.00E+00 f	2.25E+03	6.13E+03
Antimony	5.50E+00	5.50E+00	6.55E-02 c	9.01E-02	9.01E-02
Arsenic	2.20E+00	4.20E+00	3.00E-01 c	1.65E-01	3.15E-01
Barium	1.04E+02	2.80E+02	3.67E-02 c	9.56E-01	2.57E+00
Beryllium	3.07E-01	7.50E-01	1.00E+00 f	7.68E-02	1.88E-01
Cadmium	3.91E-01	4.90E-01	2.53E+01 c	2.47E+00	3.10E+00
Chromium	8.57E+00	1.98E+01	6.83E-02 d	1.46E-01	3.38E-01
Cobalt	4.84E+00	1.70E+01	3.80E-01 d	4.60E-01	1.62E+00
Copper	1.80E+01	5.10E+01	7.20E-01 c	3.23E+00	9.18E+00
Cyanide	6.36E-01	1.90E+00	1.00E+00 f	1.59E-01	4.75E-01
Iron	1.44E+04	2.94E+04	4.95E-02 c	1.78E+02	3.64E+02
Lead	2.35E+02	1.04E+03	5.68E-01 c	3.33E+01	1.48E+02
Manganese	2.54E+02	1.22E+03	4.42E-02 c	2.81E+00	1.35E+01
Mercury	1.39E-01	3.50E-01	1.08E+00 d	3.75E-02	9.45E-02
Nickel	1.99E+02	5.96E+02	1.00E+00 f	4.97E+01	1.49E+02

TABLE E-2. EARTHWORM CONCENTRATIONS OF COCS, WETLAND SOILS (cont...)

Contaminant of Concern	Soil Concentration		Earthworm	Earthworm Concentration[2]	
	Mean (mg/kg)	Maximum (mg/kg)	Bioaccumulation Factor[1]	Mean (mg/kg)	Maximum (mg/kg)
Selenium	2.84E-01	5.20E-01	5.88E+00 e	4.17E-01	7.64E-01
Thallium	1.08E-01	2.40E-01	1.00E+00 f	2.70E-02	6.00E-02
Vanadium	1.37E+01	2.52E+01	1.00E+00 f	3.43E+00	6.30E+00
Zinc	1.43E+02	5.06E+02	4.89E+00 c	1.75E+02	6.19E+02

[1] BAFs from a) Markwell et al. (1989), b) Marquenie et al. (1987 - wetland soils), c) Ireland (1983), Helmke et al. (1979), e) Beyer and Cromartie (1987), or f) no data available, therefore, assumed that earthworm concentrations equals soil concentration.

[2] Earthworm Concentration = Soil Concentration x Earthworm Bioaccumulation Factor.

Note: Earthworm concentration converted from dry weight to wet weight by multiplying by 0.25 (Beyer and Gish, 1980).

TABLE E-3. SEED CONCENTRATIONS OF COCS, WETLAND SOILS.

Contaminant of Concern	Soil Concentration		Log Kow[1]	Plant Uptake Factor[2]	Seed/Fruit Concentration[3]	
	Mean (mg/kg)	Maximum (mg/kg)			Mean (mg/kg)	Maximum (mg/kg)
Acetone	1.28E-01	1.10E+00	-0.24	1.47E-01	1.69E-02	1.46E-01
Benzene	6.05E-03	2.00E-02	2.12	7.48E-01	4.07E-03	1.35E-02
2-Butanone	4.66E-02	3.90E-01	0.26	3.04E-01	1.27E-02	1.07E-01
Carbon Disulfide	8.85E-03	3.70E-02	2.00	7.69E-01	6.13E-03	2.56E-02
1,1-Dichloroethane	6.05E-03	2.00E-02	1.79	7.84E-01	4.27E-03	1.41E-02
1,1-Dichloroethene	7.92E-03	4.80E-02	1.84	7.81E-01	5.56E-03	3.37E-02
1,2-Dichloroethene (Total)	4.52E+00	6.60E+01	0.70	4.86E-01	1.98E+00	2.89E+01
Ethyl Benzene	2.13E-02	2.30E-01	3.15	3.63E-01	6.95E-03	7.51E-02
4-Methyl-2-Pentanone	1.41E-02	6.80E-02	1.19	5.64E-01	7.13E-03	3.45E-02
Tetrachloroethene	4.24E-01	5.30E+00	2.60	5.95E-01	2.27E-01	2.84E+00
Toluene	1.12E+00	1.50E+01	2.73	5.42E-01	5.48E-01	7.32E+00
1,1,1-Trichloroethane	6.12E-03	2.10E-02	2.50	4.81E-01	2.65E-03	9.09E-03
Trichloroethene	1.38E-01	1.50E+00	2.38	6.76E-01	8.42E-02	9.13E-01
Vinyl Chloride	3.37E-01	4.90E+00	1.38	6.74E-01	2.04E-01	2.97E+00
Xylenes, Total	6.72E-02	8.40E-01	3.26	3.19E-01	1.93E-02	2.41E-01
Acenaphthylene	4.41E-01	9.10E-01	3.70	1.73E-01	6.87E-02	1.42E-01
Anthracene	5.89E-01	1.50E+00	4.45	4.22E-02	2.24E-02	5.70E-02
Benzo(a)anthracene	1.44E+00	4.90E+00	5.60	1.98E-03	2.56E-03	8.73E-03
Benzo(a)pyrene	1.36E+00	4.60E+00	6.06	4.30E-04	5.28E-04	1.78E-03
Benzo(b)fluoranthene	1.89E+00	6.70E+00	6.06	4.30E-04	7.31E-04	2.59E-03
Benzo(k)fluoranthene	1.44E+00	4.90E+00	6.06	4.30E-04	5.57E-04	1.90E-03
Chrysene	1.74E+00	6.10E+00	5.61	1.92E-03	3.00E-03	1.05E-02
Fluoranthene	3.21E+00	1.20E+01	4.90	1.45E-02	4.19E-02	1.57E-01
Indeno(1,2,3-cd)pyrene	1.04E+00	3.30E+00	6.50	8.49E-05	7.94E-05	2.52E-04
Phenanthrene	3.71E+00	1.40E+01	4.46	4.13E-02	1.38E-01	5.20E-01
Pyrene	3.21E+00	1.20E+01	4.88	1.53E-02	4.43E-02	1.65E-01
Aluminum	8.99E+03	2.45E+04	NA	6.50E-04	5.26E+00	1.43E+01
Antimony	7.88E-01	5.50E+00	NA	3.00E-02	2.13E-02	1.49E-01
Arsenic	2.39E+00	4.20E+00	NA	6.00E-03	1.29E-02	2.27E-02
Barium	7.56E+01	2.80E+02	NA	1.50E-02	1.02E+00	3.78E+00
Beryllium	3.81E-01	1.30E+00	NA	1.50E-03	5.14E-04	1.76E-03
Cadmium	3.78E-01	2.39E+00	NA	1.50E-01	5.10E-02	3.23E-01
Chromium	8.57E+00	1.98E+01	NA	4.50E-03	3.47E-02	8.02E-02
Cobalt	4.84E+00	1.70E+01	NA	7.00E-03	3.05E-02	1.07E-01
Copper	1.22E+01	5.10E+01	NA	2.50E-01	2.74E+00	1.15E+01
Cyanide	6.36E-01	1.90E+00	NA	--	0.00E+00	0.00E+00
Iron	1.34E+04	2.94E+04	NA	1.00E-03	1.21E+01	2.65E+01
Lead	1.22E+02	1.04E+03	NA	9.00E-03	9.92E-01	8.42E+00
Manganese	2.54E+02	1.22E+03	NA	5.00E-02	1.14E+01	5.49E+01
Mercury	1.25E-01	3.60E-01	NA	2.00E-01	2.25E-02	6.48E-02
Nickel	9.77E+01	5.96E+02	NA	6.00E-02	5.28E+00	3.22E+01

TABLE E-3. SEED CONCENTRATIONS OF COCS, WETLAND SOILS (cont...)

Contaminant of Concern	Soil Concentration Mean (mg/kg)	Soil Concentration Maximum (mg/kg)	Log Kow[1]	Plant Uptake Factor[2]	Seed/Fruit Concentration[3] Mean (mg/kg)	Seed/Fruit Concentration[3] Maximum (mg/kg)
Selenium	2.84E-01	5.20E-01	NA	2.50E-02	6.39E-03	1.17E-02
Thallium	1.28E-01	2.40E-01	NA	4.00E-04	4.61E-05	8.64E-05
Vanadium	1.37E+01	2.52E+01	NA	3.00E-03	3.71E-02	6.80E-02
Zinc	1.09E+02	5.06E+02	NA	9.00E-01	8.87E+01	4.10E+02

NA: Not Applicable

[1] from Superfund Public Health Evaluation Manual, 1986.

[2] Organics from Briggs et al. (1982), Inorganics from Baes et al. (1984 - reproductive portions).

[3] Plant concentration = Soil concentration x Plant uptake factor.

Note: Seed/fruit concentration converted from dry weight to wet weight by multiplying by 0.9 (Baes et al., 1984).

TABLE E-4. ESTIMATED EXPOSURE DOSES FOR MEADOW VOLE TO SOIL/PLANT INGESTION, WETLAND SOILS.

Contaminant of Concern	Soil Concentration		Plant Concentration		Daily Intake Rate	Body Weight	Soil Exposure Dose		Plant Exposure Dose		Total Exposure Dose	
	Mean (mg/kg)	Maximum (mg/kg)	Mean (mg/kg)	Maximum (mg/kg)	(kg/day)	(kg)	Mean (mg/kg/day)	Maximum (mg/kg/day)	Mean (mg/kg/day)	Maximum (mg/kg/day)	Mean (mg/kg/day)	Maximum (mg/kg/day)
Acetone	2.64E-01	1.10E+00	3.88E-03	1.62E-02	7.00E-03	2.00E-02	9.25E-04	3.85E-03	1.35E-03	5.60E-03	2.27E-03	9.45E-03
Benzene	8.36E-03	2.00E-02	6.25E-04	1.50E-03	7.00E-03	2.00E-02	2.92E-05	7.00E-05	2.17E-04	5.18E-04	2.46E-04	5.88E-04
2-Butanone	9.06E-02	3.90E-01	2.75E-03	1.19E-02	7.00E-03	2.00E-02	3.17E-04	1.37E-03	9.54E-04	4.11E-03	1.27E-03	5.47E-03
Carbon Disulfide	1.44E-02	3.70E-02	1.10E-03	2.85E-03	7.00E-03	2.00E-02	5.02E-05	1.30E-04	3.83E-04	9.86E-04	4.33E-04	1.12E-03
1,1-Dichloroethane	8.36E-03	2.00E-02	6.55E-04	1.57E-03	7.00E-03	2.00E-02	2.92E-05	7.00E-05	2.27E-04	5.43E-04	2.56E-04	6.13E-04
1,1-Dichloroethene	1.24E-02	4.80E-02	9.65E-04	3.75E-03	7.00E-03	2.00E-02	4.32E-05	1.68E-04	3.34E-04	1.30E-03	3.78E-04	1.47E-03
1,2-Dichloroethene (Total)	9.68E+00	6.60E+01	4.70E-01	3.21E+00	7.00E-03	2.00E-02	3.39E-02	2.31E-01	1.63E-01	1.11E+00	1.97E-01	1.34E+00
Ethyl Benzene	4.10E-02	2.30E-01	1.49E-03	8.35E-03	7.00E-03	2.00E-02	1.44E-04	8.05E-04	5.16E-04	2.89E-03	6.59E-04	3.70E-03
4-Methyl-2-Pentanone	2.09E-02	6.80E-02	1.18E-03	3.84E-03	7.00E-03	2.00E-02	7.30E-05	2.38E-04	4.08E-04	1.33E-03	4.81E-04	1.57E-03
Tetrachloroethene	8.88E-01	5.30E+00	5.29E-02	3.15E-01	7.00E-03	2.00E-02	3.11E-03	1.86E-02	1.83E-02	1.09E-01	2.14E-02	1.28E-01
Toluene	2.40E+00	1.50E+01	1.30E-01	8.13E-01	7.00E-03	2.00E-02	8.42E-03	5.25E-02	4.52E-02	2.82E-01	5.36E-02	3.34E-01
1,1,1-Trichloroethane	8.50E-03	2.10E-02	4.09E-04	1.01E-03	7.00E-03	2.00E-02	2.98E-05	7.35E-05	1.42E-04	3.50E-04	1.75E-02	2.47E-02
Trichloroethene	2.86E-01	1.50E+00	1.93E-02	1.01E-01	7.00E-03	2.00E-02	9.99E-04	5.25E-03	6.69E-03	3.51E-02	7.69E-03	4.04E-02
Vinyl Chloride	7.12E-01	4.90E+00	4.80E-02	3.30E-01	7.00E-03	2.00E-02	2.49E-03	1.72E-02	1.66E-02	1.14E-01	1.91E-02	1.32E-01
Xylenes, Total	1.39E-01	8.40E-01	4.44E-03	2.68E-02	7.00E-03	2.00E-02	4.88E-04	2.94E-03	1.54E-03	9.28E-03	2.03E-03	1.22E-02
Acenaphthylene	4.41E-01	9.10E-01	7.63E-03	1.57E-02	7.00E-03	2.00E-02	1.54E-03	3.19E-03	2.64E-03	5.44E-03	4.19E-03	8.63E-03
Anthracene	5.89E-01	1.50E+00	2.48E-03	6.33E-03	7.00E-03	2.00E-02	2.06E-03	5.25E-03	8.59E-04	2.19E-03	2.92E-03	7.44E-03
Benzo(a)anthracene	1.44E+00	4.90E+00	2.85E-04	9.70E-04	7.00E-03	2.00E-02	5.04E-03	1.72E-02	9.88E-05	3.36E-04	5.13E-03	1.75E-02
Benzo(a)pyrene	1.36E+00	4.60E+00	5.86E-05	1.98E-04	7.00E-03	2.00E-02	4.77E-03	1.61E-02	2.03E-05	6.86E-05	4.79E-03	1.62E-02
Benzo(b)fluoranthene	1.89E+00	6.70E+00	8.12E-05	2.88E-04	7.00E-03	2.00E-02	6.61E-03	2.35E-02	2.81E-05	9.98E-05	6.64E-03	2.35E-02
Benzo(k)fluoranthene	1.44E+00	4.90E+00	6.19E-05	2.11E-04	7.00E-03	2.00E-02	5.04E-03	1.72E-02	2.14E-05	7.31E-05	5.06E-03	1.72E-02
Chrysene	1.74E+00	6.10E+00	3.34E-04	1.17E-03	7.00E-03	2.00E-02	6.09E-03	2.14E-02	1.16E-04	4.05E-04	6.20E-03	2.18E-02
Fluoranthene	3.21E+00	1.20E+01	4.66E-03	1.74E-02	7.00E-03	2.00E-02	1.12E-02	4.20E-02	1.61E-03	6.03E-03	1.29E-02	4.80E-02
Indeno(1,2,3-cd)pyrene	1.04E+00	3.30E+00	8.82E-06	2.80E-05	7.00E-03	2.00E-02	3.64E-03	1.16E-02	3.06E-06	9.70E-06	3.64E-03	1.16E-02
Phenanthrene	3.71E+00	1.40E+01	1.53E-02	5.78E-02	7.00E-03	2.00E-02	1.30E-02	4.90E-02	5.30E-03	2.00E-02	1.83E-02	6.90E-02
Pyrene	3.21E+00	1.20E+01	4.92E-03	1.84E-02	7.00E-03	2.00E-02	1.12E-02	4.20E-02	1.70E-03	6.38E-03	1.30E-02	4.84E-02
Aluminum	8.99E+03	2.45E+04	3.60E+00	9.80E+00	7.00E-03	2.00E-02	3.15E+01	8.58E+01	1.25E+00	3.40E+00	3.27E+01	8.91E+01
Antimony	5.50E+00	5.50E+00	1.10E-01	1.10E-01	7.00E-03	2.00E-02	1.93E-02	1.93E-02	3.81E-02	3.81E-02	5.74E-02	5.74E-02
Arsenic	2.20E+00	4.20E+00	8.80E-03	1.68E-02	7.00E-03	2.00E-02	7.70E-03	1.47E-02	3.05E-03	5.82E-03	1.07E-02	2.05E-02
Barium	1.04E+02	2.80E+02	1.56E+00	4.20E+00	7.00E-03	2.00E-02	3.65E-01	9.80E-01	5.42E-01	1.46E+00	9.07E-01	2.44E+00
Beryllium	3.07E-01	7.50E-01	3.07E-04	7.50E-04	7.00E-03	2.00E-02	1.07E-03	2.63E-03	1.06E-04	2.60E-04	1.18E-03	2.88E-03
Cadmium	3.91E-01	4.90E-01	2.15E-02	2.70E-02	7.00E-03	2.00E-02	1.37E-03	1.72E-03	7.45E-03	9.34E-03	8.82E-03	1.11E-02
Chromium	8.57E+00	1.98E+01	6.43E-03	1.49E-02	7.00E-03	2.00E-02	3.00E-02	6.93E-02	2.23E-03	5.16E-03	3.22E-02	7.45E-02
Cobalt	4.84E+00	1.70E+01	9.68E-03	3.40E-02	7.00E-03	2.00E-02	1.69E-02	5.95E-02	3.35E-03	1.18E-02	2.03E-02	7.13E-02

TABLE E-4. ESTIMATED EXPOSURE DOSES FOR MEADOW VOLE TO SOIL/PLANT INGESTION, WETLAND SOILS (continued...)

Contaminant of Concern	Soil Concentration		Plant Concentration		Daily Intake Rate (kg/day)	Body Weight (kg)	Soil Exposure Dose		Plant Exposure Dose		Total Exposure Dose	
	Mean (mg/kg)	Maximum (mg/kg)	Mean (mg/kg)	Maximum (mg/kg)			Mean (mg/kg/day)	Maximum (mg/kg/day)	Mean (mg/kg/day)	Maximum (mg/kg/day)	Mean (mg/kg/day)	Maximum (mg/kg/day)
Copper	1.80E+01	5.10E+01	7.18E-01	2.04E+00	7.00E-03	2.00E-02	6.28E-02	1.79E-01	2.49E-01	7.07E-01	3.12E-01	8.85E-01
Cyanide	6.36E-01	1.90E+00	--	--	7.00E-03	2.00E-02	2.23E-03	6.65E-03	0.00E+00	0.00E+00	2.23E-03	6.65E-03
Iron	1.44E+04	2.94E+04	5.77E+00	1.18E+01	7.00E-03	2.00E-02	5.05E+01	1.03E+02	2.00E+00	4.07E+00	5.25E+01	1.07E+02
Lead	2.35E+02	1.04E+03	1.06E+00	4.68E+00	7.00E-03	2.00E-02	8.21E-01	3.64E+00	3.66E-01	1.62E+00	1.19E+00	5.26E+00
Manganese	2.54E+02	1.22E+03	6.36E+00	3.05E+01	7.00E-03	2.00E-02	8.89E-01	4.27E+00	2.20E+00	1.06E+01	3.09E+00	1.48E+01
Mercury	1.39E-01	3.50E-01	1.25E-02	3.15E-02	7.00E-03	2.00E-02	4.87E-04	1.23E-03	4.33E-03	1.09E-02	4.82E-03	1.21E-02
Nickel	1.99E+02	5.96E+02	1.19E+00	3.58E+00	7.00E-03	2.00E-02	6.96E-01	2.09E+00	4.13E-01	1.24E+00	1.11E+00	3.33E+00
Selenium	2.84E-01	5.20E-01	7.10E-04	1.30E-03	7.00E-03	2.00E-02	9.94E-04	1.82E-03	2.46E-04	4.50E-04	1.24E-03	2.27E-03
Thallium	1.08E-01	2.40E-01	4.32E-05	9.60E-05	7.00E-03	2.00E-02	3.78E-04	8.40E-04	1.50E-05	3.33E-05	3.93E-04	8.73E-04
Vanadium	1.37E+01	2.52E+01	7.56E-03	1.39E-02	7.00E-03	2.00E-02	4.80E-02	8.82E-02	2.62E-03	4.82E-03	5.06E-02	9.30E-02
Zinc	1.43E+02	5.06E+02	2.15E+01	7.59E+01	7.00E-03	2.00E-02	5.02E-01	1.77E+00	7.45E+00	2.63E+01	7.96E+00	2.81E+01

TABLE E-5. ESTIMATED EXPOSURE DOSES FOR SHORT-TAILED SHREW TO SOIL/EARTHWORM INGESTION, WETLANDS SOIL.

	Soil Concentration		Worm Concentratio		Daily	Body	Soil Exposure Dose		Worm Exposure Dose		Total Exposure Dose	
Contaminant of Concern	Mean (mg/kg)	Maximum (mg/kg)	Mean (mg/kg)	Maximum (mg/kg)	Intake Rate (kg/day)	Weight (kg)	Mean (mg/kg/day)	Maximum (mg/kg/day)	Mean (mg/kg/day)	Maximum (mg/kg/day)	Mean (mg/kg/day)	Maximum (mg/kg/day)
Acetone	2.64E-01	1.10E+00	1.02E-01	4.24E-01	2.00E-03	1.52E-02	1.74E-03	7.24E-03	1.27E-02	5.29E-02	1.44E-02	6.02E-02
Benzene	8.36E-03	2.00E-02	5.01E-03	1.20E-02	2.00E-03	1.52E-02	5.50E-05	1.32E-04	6.27E-04	1.50E-03	6.82E-04	1.63E-03
2-Butanone	9.06E-02	3.90E-01	3.83E-02	1.65E-01	2.00E-03	1.52E-02	5.96E-04	2.57E-03	4.78E-03	2.06E-02	5.38E-03	2.32E-02
Carbon Disulfide	1.44E-02	3.70E-02	8.40E-03	2.16E-02	2.00E-03	1.52E-02	9.45E-05	2.43E-04	1.05E-03	2.71E-03	1.14E-03	2.95E-03
1,1-Dichloroethane	8.36E-03	2.00E-02	4.70E-03	1.13E-02	2.00E-03	1.52E-02	5.50E-05	1.32E-04	5.88E-04	1.41E-03	6.43E-04	1.54E-03
1,1-Dichloroethene	1.24E-02	4.80E-02	7.01E-03	2.72E-02	2.00E-03	1.52E-02	8.13E-05	3.16E-04	8.77E-04	3.41E-03	9.58E-04	3.72E-03
1,2-Dichloroethene (Total)	9.68E+00	6.60E+01	4.45E+00	3.04E+01	2.00E-03	1.52E-02	6.37E-02	4.34E-01	5.56E-01	3.80E+00	6.20E-01	4.23E+00
Ethyl Benzene	4.10E-02	2.30E-01	2.97E-02	1.67E-01	2.00E-03	1.52E-02	2.70E-04	1.51E-03	3.72E-03	2.08E-02	3.99E-03	2.24E-02
4-Methyl-2-Pentanone	2.09E-02	6.80E-02	1.05E-02	3.42E-02	2.00E-03	1.52E-02	1.37E-04	4.47E-04	1.31E-03	4.27E-03	1.45E-03	4.72E-03
Tetrachloroethene	8.88E-01	5.30E+00	5.82E-01	3.47E+00	2.00E-03	1.52E-02	5.84E-03	3.49E-02	7.27E-02	4.34E-01	7.86E-02	4.69E-01
Toluene	2.40E+00	1.50E+01	1.61E+00	1.01E+01	2.00E-03	1.52E-02	1.58E-02	9.87E-02	2.01E-01	1.26E+00	2.17E-01	1.35E+00
1,1,1-Trichloroethane	8.50E-03	2.10E-02	5.46E-03	1.35E-02	2.00E-03	1.52E-02	5.59E-05	1.38E-04	6.83E-04	1.69E-03	7.39E-04	1.82E-03
Trichloroethene	2.86E-01	1.50E+00	1.80E-01	9.45E-01	2.00E-03	1.52E-02	1.88E-03	9.87E-03	2.25E-02	1.18E-01	2.44E-02	1.28E-01
Vinyl Chloride	7.12E-01	4.90E+00	3.72E-01	2.56E+00	2.00E-03	1.52E-02	4.69E-03	3.22E-02	4.65E-02	3.20E-01	5.12E-02	3.52E-01
Xylenes, Total	1.39E-01	8.40E-01	1.03E-01	6.22E-01	2.00E-03	1.52E-02	9.16E-04	5.53E-03	1.29E-02	7.77E-02	1.38E-02	8.32E-02
Acenaphthylene	4.41E-01	9.10E-01	1.10E-01	2.28E-01	2.00E-03	1.52E-02	2.90E-03	5.99E-03	1.38E-02	2.84E-02	1.67E-02	3.44E-02
Anthracene	5.89E-01	1.50E+00	1.22E-02	3.11E-02	2.00E-03	1.52E-02	3.87E-03	9.87E-03	1.53E-03	3.89E-03	5.40E-03	1.38E-02
Benzo(a)anthracene	1.44E+00	4.90E+00	6.69E-02	2.28E-01	2.00E-03	1.52E-02	9.47E-03	3.22E-02	8.36E-03	2.85E-02	1.78E-02	6.07E-02
Benzo(a)pyrene	1.36E+00	4.60E+00	2.12E-01	7.16E-01	2.00E-03	1.52E-02	8.97E-03	3.03E-02	2.66E-02	8.96E-02	3.55E-02	1.20E-01
Benzo(b)fluoranthene	1.89E+00	6.70E+00	3.37E-01	1.19E+00	2.00E-03	1.52E-02	1.24E-02	4.41E-02	4.21E-02	1.49E-01	5.45E-02	1.93E-01
Benzo(k)fluoranthene	1.44E+00	4.90E+00	2.24E-01	7.63E-01	2.00E-03	1.52E-02	9.47E-03	3.22E-02	2.80E-02	9.54E-02	3.75E-02	1.28E-01
Chrysene	1.74E+00	6.10E+00	1.31E-01	4.61E-01	2.00E-03	1.52E-02	1.14E-02	4.01E-02	1.64E-02	5.76E-02	2.78E-02	9.77E-02
Fluoranthene	3.21E+00	1.20E+01	1.18E-01	4.41E-01	2.00E-03	1.52E-02	2.11E-02	7.89E-02	1.48E-02	5.51E-02	3.59E-02	1.34E-01
Indeno(1,2,3-cd)pyrene	1.04E+00	3.30E+00	1.37E-01	4.36E-01	2.00E-03	1.52E-02	6.83E-03	2.17E-02	1.72E-02	5.46E-02	2.40E-02	7.63E-02
Phenanthrene	3.71E+00	1.40E+01	1.64E-01	6.20E-01	2.00E-03	1.52E-02	2.44E-02	9.21E-02	2.05E-02	7.74E-02	4.50E-02	1.70E-01
Pyrene	3.21E+00	1.20E+01	2.22E-01	8.28E-01	2.00E-03	1.52E-02	2.11E-02	7.89E-02	2.77E-02	1.04E-01	4.89E-02	1.82E-01
Aluminum	8.99E+03	2.45E+04	2.25E+03	6.13E+03	2.00E-03	1.52E-02	5.91E+01	1.61E+02	2.81E+02	7.66E+02	3.40E+02	9.27E+02
Antimony	5.50E+00	5.50E+00	9.01E-02	9.01E-02	2.00E-03	1.52E-02	3.62E-02	3.62E-02	1.13E-02	1.13E-02	4.74E-02	4.74E-02
Arsenic	2.20E+00	4.20E+00	1.65E-01	3.15E-01	2.00E-03	1.52E-02	1.45E-02	2.76E-02	2.06E-02	3.94E-02	3.51E-02	6.70E-02
Barium	1.04E+02	2.80E+02	9.56E-01	2.57E+00	2.00E-03	1.52E-02	6.86E-01	1.84E+00	1.20E-01	3.21E-01	8.05E-01	2.16E+00
Beryllium	3.07E-01	7.50E-01	7.68E-02	1.88E-01	2.00E-03	1.52E-02	2.02E-03	4.93E-03	9.59E-03	2.34E-02	1.16E-02	2.84E-02
Cadmium	3.91E-01	4.90E-01	2.47E+00	3.10E+00	2.00E-03	1.52E-02	2.57E-03	3.22E-03	3.09E-01	3.87E-01	3.12E-01	3.91E-01
Chromium	8.57E+00	1.98E+01	1.46E-01	3.38E-01	2.00E-03	1.52E-02	5.64E-02	1.30E-01	1.83E-02	4.23E-02	7.46E-02	1.73E-01
Cobalt	4.84E+00	1.70E+01	4.60E-01	1.62E+00	2.00E-03	1.52E-02	3.18E-02	1.12E-01	5.75E-02	2.03E-01	8.93E-02	3.14E-01

TABLE E-5. ESTIMATED EXPOSURE DOSES FOR SHORT-TAILED SHREW TO SOIL/EARTHWORM INGESTION, WETLANDS SOIL (cont...)

Contaminant of Concern	Soil Concentration		Worm Concentration		Daily Intake Rate	Body Weight	Soil Exposure Dose		Worm Exposure Dose		Total Exposure Dose	
	Mean (mg/kg)	Maximum (mg/kg)	Mean (mg/kg)	Maximum (mg/kg)	(kg/day)	(kg)	Mean (mg/kg/day)	Maximum (mg/kg/day)	Mean (mg/kg/day)	Maximum (mg/kg/day)	Mean (mg/kg/day)	Maximum (mg/kg/day)
Copper	1.80E+01	5.10E+01	3.23E+00	9.18E+00	2.00E-03	1.52E-02	1.18E-01	3.36E-01	4.04E-01	1.15E+00	5.22E-01	1.48E+00
Cyanide	6.36E-01	1.90E+00	1.59E-01	4.75E-01	2.00E-03	1.52E-02	4.18E-03	1.25E-02	1.99E-02	5.94E-02	2.41E-02	7.19E-02
Iron	1.44E+04	2.94E+04	1.78E+02	3.64E+02	2.00E-03	1.52E-02	9.48E+01	1.93E+02	2.23E+01	4.55E+01	1.17E+02	2.39E+02
Lead	2.35E+02	1.04E+03	3.33E+01	1.48E+02	2.00E-03	1.52E-02	1.54E+00	6.84E+00	4.16E+00	1.85E+01	5.71E+00	2.53E+01
Manganese	2.54E+02	1.22E+03	2.81E+00	1.35E+01	2.00E-03	1.52E-02	1.67E+00	8.03E+00	3.51E-01	1.69E+00	2.02E+00	9.71E+00
Mercury	1.39E-01	3.50E-01	3.75E-02	9.45E-02	2.00E-03	1.52E-02	9.14E-04	2.30E-03	4.69E-03	1.18E-02	5.61E-03	1.41E-02
Nickel	1.99E+02	5.96E+02	4.97E+01	1.49E+02	2.00E-03	1.52E-02	1.31E+00	3.92E+00	6.21E+00	1.86E+01	7.52E+00	2.25E+01
Selenium	2.84E-01	5.20E-01	4.17E-01	7.64E-01	2.00E-03	1.52E-02	1.87E-03	3.42E-03	5.21E-02	9.55E-02	5.40E-02	9.89E-02
Thallium	1.08E-01	2.40E-01	2.70E-02	6.00E-02	2.00E-03	1.52E-02	7.11E-04	1.58E-03	3.38E-03	7.50E-03	4.09E-03	9.08E-03
Vanadium	1.37E+01	2.52E+01	3.43E+00	6.30E+00	2.00E-03	1.52E-02	9.01E-02	1.66E-01	4.29E-01	7.88E-01	5.19E-01	9.53E-01
Zinc	1.43E+02	5.06E+02	1.75E+02	6.19E+02	2.00E-03	1.52E-02	9.44E-01	3.33E+00	2.19E+01	7.73E+01	2.29E+01	8.07E+01

TABLE E-6. ESTIMATED EXPOSURE DOSES FOR AMERICAN ROBIN TO INVERTEBRATE/SEED INGESTION, WETLAND SOILS.

Contaminant of Concern	Invertebrate Conc.		Seed Concentration		Daily Intake Rate	Body Weight	Invert. Exposure Dose		Seed Exposure Dose		Food Exposure Dose	
	Mean (mg/kg)	Maximum (mg/kg)	Mean (mg/kg)	Maximum (mg/kg)	(kg/day)	(kg)	Mean (mg/kg/day)	Maximum (mg/kg/day)	Mean (mg/kg/day)	Maximum (mg/kg/day)	Mean (mg/kg/day)	Maximum (mg/kg/day)
Acetone	1.02E-01	4.24E-01	1.69E-02	1.46E-01	6.08E-02	7.73E-02	7.20E-02	3.00E-01	1.33E-03	1.14E-02	7.33E-02	3.11E-01
Benzene	5.01E-03	1.20E-02	4.07E-03	1.35E-02	6.08E-02	7.73E-02	3.55E-03	8.49E-03	3.20E-04	1.06E-03	3.87E-03	9.55E-03
2-Butanone	3.83E-02	1.65E-01	1.27E-02	1.07E-01	6.08E-02	7.73E-02	2.71E-02	1.17E-01	1.00E-03	8.39E-03	2.81E-02	1.25E-01
Carbon Disulfide	8.40E-03	2.16E-02	6.13E-03	2.56E-02	6.08E-02	7.73E-02	5.95E-03	1.53E-02	4.82E-04	2.01E-03	6.43E-03	1.73E-02
1,1-Dichloroethane	4.70E-03	1.13E-02	4.27E-03	1.41E-02	6.08E-02	7.73E-02	3.33E-03	7.96E-03	3.36E-04	1.11E-03	3.66E-03	9.07E-03
1,1-Dichloroethene	7.01E-03	2.72E-02	5.56E-03	3.37E-02	6.08E-02	7.73E-02	4.96E-03	1.93E-02	4.38E-04	2.65E-03	5.40E-03	2.19E-02
1,2-Dichloroethene (Total)	4.45E+00	3.04E+01	1.98E+00	2.89E+01	6.08E-02	7.73E-02	3.15E+00	2.15E+01	1.55E-01	2.27E+00	3.31E+00	2.38E+01
Ethyl Benzene	2.97E-02	1.67E-01	6.95E-03	7.51E-02	6.08E-02	7.73E-02	2.10E-02	1.18E-01	5.47E-04	5.91E-03	2.16E-02	1.24E-01
4-Methyl-2-Pentanone	1.05E-02	3.42E-02	7.13E-03	3.45E-02	6.08E-02	7.73E-02	7.42E-03	2.42E-02	5.61E-04	2.71E-03	7.98E-03	2.69E-02
Tetrachloroethene	5.82E-01	3.47E+00	2.27E-01	2.84E+00	6.08E-02	7.73E-02	4.12E-01	2.46E+00	1.79E-02	2.23E-01	4.30E-01	2.68E+00
Toluene	1.61E+00	1.01E+01	5.48E-01	7.32E+00	6.08E-02	7.73E-02	1.14E+00	7.11E+00	4.31E-02	5.76E-01	1.18E+00	7.69E+00
1,1,1-Trichloroethane	5.46E-03	1.35E-02	2.65E-03	9.09E-03	6.08E-02	7.73E-02	3.87E-03	9.55E-03	2.08E-04	7.15E-04	1.75E-02	2.47E-02
Trichloroethene	1.80E-01	9.45E-01	8.42E-02	9.13E-01	6.08E-02	7.73E-02	1.27E-01	6.69E-01	6.62E-03	7.18E-02	1.34E-01	7.41E-01
Vinyl Chloride	3.72E-01	2.56E+00	2.04E-01	2.97E+00	6.08E-02	7.73E-02	2.63E-01	1.81E+00	1.61E-02	2.34E-01	2.79E-01	2.05E+00
Xylenes, Total	1.03E-01	6.22E-01	1.93E-02	2.41E-01	6.08E-02	7.73E-02	7.30E-02	4.40E-01	1.52E-03	1.90E-02	7.45E-02	4.59E-01
Acenaphthylene	1.10E-01	2.28E-01	6.87E-02	1.42E-01	6.08E-02	7.73E-02	7.81E-02	1.61E-01	5.40E-03	1.11E-02	8.35E-02	1.72E-01
Anthracene	1.22E-02	3.11E-02	2.24E-02	5.70E-02	6.08E-02	7.73E-02	8.65E-03	2.20E-02	1.76E-03	4.48E-03	1.04E-02	2.65E-02
Benzo(a)anthracene	6.69E-02	2.28E-01	2.56E-03	8.73E-03	6.08E-02	7.73E-02	4.74E-02	1.61E-01	2.02E-04	6.87E-04	4.76E-02	1.62E-01
Benzo(a)pyrene	2.12E-01	7.16E-01	5.28E-04	1.78E-03	6.08E-02	7.73E-02	1.50E-01	5.07E-01	4.15E-05	1.40E-04	1.50E-01	5.07E-01
Benzo(b)fluoranthene	3.37E-01	1.19E+00	7.31E-04	2.59E-03	6.08E-02	7.73E-02	2.38E-01	8.45E-01	5.75E-05	2.04E-04	2.38E-01	8.46E-01
Benzo(k)fluoranthene	2.24E-01	7.63E-01	5.57E-04	1.90E-03	6.08E-02	7.73E-02	1.59E-01	5.40E-01	4.38E-05	1.49E-04	1.59E-01	5.40E-01
Chrysene	1.31E-01	4.61E-01	3.00E-03	1.05E-02	6.08E-02	7.73E-02	9.29E-02	3.26E-01	2.36E-04	8.29E-04	9.32E-02	3.27E-01
Fluoranthene	1.18E-01	4.41E-01	4.19E-02	1.57E-01	6.08E-02	7.73E-02	8.36E-02	3.12E-01	3.30E-03	1.23E-02	8.69E-02	3.24E-01
Indeno(1,2,3-cd)pyrene	1.37E-01	4.36E-01	7.94E-05	2.52E-04	6.08E-02	7.73E-02	9.72E-02	3.09E-01	6.24E-06	1.98E-05	9.73E-02	3.09E-01
Phenanthrene	1.64E-01	6.20E-01	1.38E-01	5.20E-01	6.08E-02	7.73E-02	1.16E-01	4.39E-01	1.09E-02	4.09E-02	1.27E-01	4.79E-01
Pyrene	2.22E-01	8.28E-01	4.43E-02	1.65E-01	6.08E-02	7.73E-02	1.57E-01	5.86E-01	3.48E-03	1.30E-02	1.60E-01	5.99E-01
Aluminum	2.25E+03	6.13E+03	5.26E+00	1.43E+01	6.08E-02	7.73E-02	1.59E+03	4.34E+03	4.14E-01	1.13E+00	1.59E+03	4.34E+03
Antimony	9.01E-02	9.01E-02	2.13E-02	1.49E-01	6.08E-02	7.73E-02	6.38E-02	6.38E-02	1.67E-03	1.17E-02	6.54E-02	7.54E-02
Arsenic	1.65E-01	3.15E-01	1.29E-02	2.27E-02	6.08E-02	7.73E-02	1.17E-01	2.23E-01	1.02E-03	1.78E-03	1.18E-01	2.25E-01
Barium	9.56E-01	2.57E+00	1.02E+00	3.78E+00	6.08E-02	7.73E-02	6.77E-01	1.82E+00	8.02E-02	2.97E-01	7.57E-01	2.12E+00
Beryllium	7.68E-02	1.88E-01	5.14E-04	1.76E-03	6.08E-02	7.73E-02	5.43E-02	1.33E-01	4.05E-05	1.38E-04	5.44E-02	1.33E-01
Cadmium	2.47E+00	3.10E+00	5.10E-02	3.23E-01	6.08E-02	7.73E-02	1.75E+00	2.19E+00	4.01E-03	2.54E-02	1.75E+00	2.22E+00
Chromium	1.46E-01	3.38E-01	3.47E-02	8.02E-02	6.08E-02	7.73E-02	1.04E-01	2.39E-01	2.73E-03	6.31E-03	1.06E-01	2.46E-01
Cobalt	4.60E-01	1.62E+00	3.05E-02	1.07E-01	6.08E-02	7.73E-02	3.25E-01	1.14E+00	2.40E-03	8.42E-03	3.28E-01	1.15E+00

TABLE E-6. ESTIMATED EXPOSURE DOSES FOR AMERICAN ROBIN TO INVERTEBRATE/SEED INGESTION, WETLAND SOILS (continued...)

Contaminant of Concern	Invertebrate Conc.		Seed Concentration		Daily Intake Rate	Body Weight	Invert. Exposure Dose		Seed Exposure Dose		Food Exposure Dose	
	Mean (mg/kg)	Maximum (mg/kg)	Mean (mg/kg)	Maximum (mg/kg)	(kg/day)	(kg)	Mean (mg/kg/day)	Maximum (mg/kg/day)	Mean (mg/kg/day)	Maximum (mg/kg/day)	Mean (mg/kg/day)	Maximum (mg/kg/day)
Copper	3.23E+00	9.18E+00	2.74E+00	1.15E+01	6.08E-02	7.73E-02	2.29E+00	6.50E+00	2.15E-01	9.03E-01	2.50E+00	7.40E+00
Cyanide	1.59E-01	4.75E-01	0.00E+00	0.00E+00	6.08E-02	7.73E-02	1.13E-01	3.36E-01	0.00E+00	0.00E+00	1.13E-01	3.36E-01
Iron	1.78E+02	3.64E+02	1.21E+01	2.65E+01	6.08E-02	7.73E-02	1.26E+02	2.58E+02	9.49E-01	2.08E+00	1.27E+02	2.60E+02
Lead	3.33E+01	1.48E+02	9.92E-01	8.42E+00	6.08E-02	7.73E-02	2.36E+01	1.05E+02	7.80E-02	6.63E-01	2.37E+01	1.05E+02
Manganese	2.81E+00	1.35E+01	1.14E+01	5.49E+01	6.08E-02	7.73E-02	1.99E+00	9.54E+00	9.00E-01	4.32E+00	2.89E+00	1.39E+01
Mercury	3.75E-02	9.45E-02	2.25E-02	6.48E-02	6.08E-02	7.73E-02	2.66E-02	6.69E-02	1.77E-03	5.10E-03	2.83E-02	7.20E-02
Nickel	4.97E+01	1.49E+02	5.28E+00	3.22E+01	6.08E-02	7.73E-02	3.52E+01	1.05E+02	4.15E-01	2.53E+00	3.56E+01	1.08E+02
Selenium	4.17E-01	7.64E-01	6.39E-03	1.17E-02	6.08E-02	7.73E-02	2.96E-01	5.41E-01	5.03E-04	9.20E-04	2.96E-01	5.42E-01
Thallium	2.70E-02	6.00E-02	4.61E-05	8.64E-05	6.08E-02	7.73E-02	1.91E-02	4.25E-02	3.62E-06	6.80E-06	1.91E-02	4.25E-02
Vanadium	3.43E+00	6.30E+00	3.71E-02	6.80E-02	6.08E-02	7.73E-02	2.42E+00	4.46E+00	2.92E-03	5.35E-03	2.43E+00	4.47E+00
Zinc	1.75E+02	6.19E+02	8.87E+01	4.10E+02	6.08E-02	7.73E-02	1.24E+02	4.38E+02	6.97E+00	3.22E+01	1.31E+02	4.70E+02

TABLE E-7. ESTIMATED EXPOSURE DOSES FOR AMERICAN ROBIN TO LEACHATE/SURFACE WATER INGESTION.

Contaminant of Concern	Leachate Conc.		Surface Water Conc.		Daily Intake Rate	Body Weight	Leachate Dose		Surface Water Dose		Total Water Dose	
	Mean (mg/L)	Maximum (mg/L)	Mean (mg/kg)	Maximum (mg/kg)	(L/day)	(kg)	Mean (mg/kg/day)	Maximum (mg/kg/day)	Mean (mg/kg/day)	Maximum (mg/kg/day)	Mean (mg/kg/day)	Maximum (mg/kg/day)
Acetone	2.10E-02	2.10E-02	5.08E-03	1.20E-02	1.10E-02	7.73E-02	1.49E-03	1.49E-03	3.61E-04	8.54E-04	7.33E-02	3.11E-01
Benzene	0.00E+00	0.00E+00	0.00E+00	0.00E+00	1.10E-02	7.73E-02	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
2-Butanone	0.00E+00	0.00E+00	0.00E+00	0.00E+00	1.10E-02	7.73E-02	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
Carbon Disulfide	0.00E+00	0.00E+00	3.00E-03	3.30E-02	1.10E-02	7.73E-02	0.00E+00	0.00E+00	2.13E-04	2.35E-03	2.13E-04	2.35E-03
1,1-Dichloroethane	0.00E+00	0.00E+00	0.00E+00	0.00E+00	1.10E-02	7.73E-02	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
1,1-Dichloroethene	0.00E+00	0.00E+00	1.86E-03	8.00E-03	1.10E-02	7.73E-02	0.00E+00	0.00E+00	1.32E-04	5.69E-04	1.32E-04	5.69E-04
1,2-Dichloroethene (Total)	6.14E-01	1.80E+00	1.95E-01	2.62E+00	1.10E-02	7.73E-02	4.37E-02	1.28E-01	1.38E-02	1.87E-01	5.75E-02	3.15E-01
Ethyl Benzene	0.00E+00	0.00E+00	8.00E-04	8.00E-04	1.10E-02	7.73E-02	0.00E+00	0.00E+00	5.69E-05	5.69E-05	5.69E-05	5.69E-05
4-Methyl-2-Pentanone	0.00E+00	0.00E+00	4.02E-03	1.40E-02	1.10E-02	7.73E-02	0.00E+00	0.00E+00	2.86E-04	9.96E-04	2.86E-04	9.96E-04
Tetrachloroethene	3.11E+00	9.30E+00	1.01E-02	9.70E-02	1.10E-02	7.73E-02	2.21E-01	6.62E-01	7.17E-04	6.90E-03	2.22E-01	6.69E-01
Toluene	0.00E+00	0.00E+00	2.70E-03	1.80E-02	1.10E-02	7.73E-02	0.00E+00	0.00E+00	1.92E-04	1.28E-03	1.92E-04	1.28E-03
1,1,1-Trichloroethane	0.00E+00	0.00E+00	6.00E-04	6.00E-04	1.10E-02	7.73E-02	0.00E+00	0.00E+00	4.27E-05	4.27E-05	4.27E-05	4.27E-05
Trichloroethene	8.86E+00	2.60E+01	6.98E-02	9.20E-01	1.10E-02	7.73E-02	6.30E-01	1.85E+00	4.97E-03	6.55E-02	6.35E-01	1.92E+00
Vinyl Chloride	0.00E+00	0.00E+00	4.41E-02	4.90E-01	1.10E-02	7.73E-02	0.00E+00	0.00E+00	3.14E-03	3.49E-02	3.14E-03	3.49E-02
Xylenes, Total	0.00E+00	0.00E+00	1.65E-03	3.00E-03	1.10E-02	7.73E-02	0.00E+00	0.00E+00	1.17E-04	2.13E-04	1.17E-04	2.13E-04
Acenaphthylene	0.00E+00	0.00E+00	0.00E+00	0.00E+00	1.10E-02	7.73E-02	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
Anthracene	0.00E+00	0.00E+00	0.00E+00	0.00E+00	1.10E-02	7.73E-02	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
Benzo(a)anthracene	0.00E+00	0.00E+00	0.00E+00	0.00E+00	1.10E-02	7.73E-02	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
Benzo(a)pyrene	0.00E+00	0.00E+00	0.00E+00	0.00E+00	1.10E-02	7.73E-02	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
Benzo(b)fluoranthene	0.00E+00	0.00E+00	0.00E+00	0.00E+00	1.10E-02	7.73E-02	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
Benzo(k)fluoranthene	0.00E+00	0.00E+00	0.00E+00	0.00E+00	1.10E-02	7.73E-02	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
Chrysene	0.00E+00	0.00E+00	0.00E+00	0.00E+00	1.10E-02	7.73E-02	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
Fluoranthene	0.00E+00	0.00E+00	0.00E+00	0.00E+00	1.10E-02	7.73E-02	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
Indeno(1,2,3-cd)pyrene	0.00E+00	0.00E+00	0.00E+00	0.00E+00	1.10E-02	7.73E-02	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
Phenanthrene	0.00E+00	0.00E+00	0.00E+00	0.00E+00	1.10E-02	7.73E-02	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
Pyrene	0.00E+00	0.00E+00	0.00E+00	0.00E+00	1.10E-02	7.73E-02	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
Aluminum	2.85E+01	5.31E+01	2.65E-01	2.14E+00	1.10E-02	7.73E-02	2.02E+00	3.78E+00	1.88E-02	1.52E-01	2.04E+00	3.93E+00
Antimony	1.96E-02	3.97E-02	1.93E-02	2.90E-02	1.10E-02	7.73E-02	1.39E-03	2.82E-03	1.37E-03	2.06E-03	2.77E-03	4.89E-03
Arsenic	0.00E+00	0.00E+00	1.88E-03	1.00E-02	1.10E-02	7.73E-02	0.00E+00	0.00E+00	1.34E-04	7.12E-04	1.34E-04	7.12E-04
Barium	4.06E-01	8.80E-01	7.57E-02	9.80E-01	1.10E-02	7.73E-02	2.89E-02	6.26E-02	5.38E-03	6.97E-02	3.43E-02	1.32E-01
Beryllium	1.42E-03	2.60E-03	0.00E+00	0.00E+00	1.10E-02	7.73E-02	1.01E-04	1.85E-04	0.00E+00	0.00E+00	1.01E-04	1.85E-04
Cadmium	1.43E-03	2.30E-03	4.70E-04	4.70E-04	1.10E-02	7.73E-02	1.02E-04	1.64E-04	3.34E-05	3.34E-05	1.35E-04	1.97E-04
Chromium	2.64E-02	4.31E-02	3.89E-03	3.40E-02	1.10E-02	7.73E-02	1.88E-03	3.07E-03	2.77E-04	2.42E-03	2.16E-03	5.49E-03
Cobalt	2.33E-02	4.70E-02	3.99E-03	2.56E-02	1.10E-02	7.73E-02	1.66E-03	3.34E-03	2.84E-04	1.82E-03	1.94E-03	5.17E-03

TABLE E-8. ESTIMATED TOTAL EXPOSURE DOSE FOR AMERICAN ROBIN.

Contaminant of Concern	Total Food Dose[1]		Total Water Dose[2]		Total Exposure Dose[3]	
	Mean (mg/kg/day)	Maximum (mg/kg/day)	Mean (mg/kg/day)	Maximum (mg/kg/day)	Mean (mg/kg/day)	Maximum (mg/kg/day)
Acetone	7.33E-02	3.11E-01	1.86E-03	2.35E-03	7.52E-02	3.14E-01
Benzene	3.87E-03	9.55E-03	0.00E+00	0.00E+00	3.87E-03	9.55E-03
2-Butanone	2.81E-02	1.25E-01	0.00E+00	0.00E+00	2.81E-02	1.25E-01
Carbon Disulfide	6.43E-03	1.73E-02	2.13E-04	2.35E-03	6.64E-03	1.97E-02
1,1-Dichloroethane	3.66E-03	9.07E-03	0.00E+00	0.00E+00	3.66E-03	9.07E-03
1,1-Dichloroethene	5.40E-03	2.19E-02	1.32E-04	5.69E-04	5.53E-03	2.25E-02
1,2-Dichloroethene (Total)	3.31E+00	2.38E+01	5.75E-02	3.15E-01	3.36E+00	2.41E+01
Ethyl Benzene	2.16E-02	1.24E-01	5.69E-05	5.69E-05	2.16E-02	1.24E-01
4-Methyl-2-Pentanone	7.98E-03	2.69E-02	2.86E-04	9.96E-04	8.27E-03	2.79E-02
Tetrachloroethene	4.30E-01	2.68E+00	2.22E-01	6.69E-01	6.51E-01	3.35E+00
Toluene	1.18E+00	7.69E+00	1.92E-04	1.28E-03	1.18E+00	7.69E+00
1,1,1-Trichloroethane	1.75E-02	2.47E-02	4.27E-05	4.27E-05	1.75E-02	2.47E-02
Trichloroethene	1.34E-01	7.41E-01	6.35E-01	1.92E+00	7.69E-01	2.66E+00
Vinyl Chloride	2.79E-01	2.05E+00	3.14E-03	3.49E-02	2.83E-01	2.08E+00
Xylenes, Total	7.45E-02	4.59E-01	1.17E-04	2.13E-04	7.46E-02	4.59E-01
Acenaphthylene	8.35E-02	1.72E-01	0.00E+00	0.00E+00	8.35E-02	1.72E-01
Anthracene	1.04E-02	2.65E-02	0.00E+00	0.00E+00	1.04E-02	2.65E-02
Benzo(a)anthracene	4.76E-02	1.62E-01	0.00E+00	0.00E+00	4.76E-02	1.62E-01
Benzo(a)pyrene	1.50E-01	5.07E-01	0.00E+00	0.00E+00	1.50E-01	5.07E-01
Benzo(b)fluoranthene	2.38E-01	8.46E-01	0.00E+00	0.00E+00	2.38E-01	8.46E-01
Benzo(k)fluoranthene	1.59E-01	5.40E-01	0.00E+00	0.00E+00	1.59E-01	5.40E-01
Chrysene	9.32E-02	3.27E-01	0.00E+00	0.00E+00	9.32E-02	3.27E-01
Fluoranthene	8.69E-02	3.24E-01	0.00E+00	0.00E+00	8.69E-02	3.24E-01
Indeno(1,2,3-cd)pyrene	9.73E-02	3.09E-01	0.00E+00	0.00E+00	9.73E-02	3.09E-01
Phenanthrene	1.27E-01	4.79E-01	0.00E+00	0.00E+00	1.27E-01	4.79E-01
Pyrene	1.60E-01	5.99E-01	0.00E+00	0.00E+00	1.60E-01	5.99E-01
Total PAHS	1.25E+00	4.29E+00	0.00E+00	0.00E+00	1.25E+00	4.29E+00
Aluminum	1.59E+03	4.34E+03	2.04E+00	3.93E+00	1.59E+03	4.34E+03
Antimony	6.54E-02	7.54E-02	2.77E-03	4.89E-03	6.82E-02	8.03E-02
Arsenic	1.18E-01	2.25E-01	1.34E-04	7.12E-04	1.18E-01	2.25E-01
Barium	7.57E-01	2.12E+00	3.43E-02	1.32E-01	7.92E-01	2.25E+00
Beryllium	5.44E-02	1.33E-01	1.01E-04	1.85E-04	5.45E-02	1.33E-01
Cadmium	1.75E+00	2.22E+00	1.35E-04	1.97E-04	1.75E+00	2.22E+00
Chromium	1.06E-01	2.46E-01	2.16E-03	5.49E-03	1.08E-01	2.51E-01
Cobalt	3.28E-01	1.15E+00	1.94E-03	5.17E-03	3.30E-01	1.16E+00
Copper	2.50E+00	7.40E+00	7.14E-03	1.55E-02	2.51E+00	7.42E+00
Cyanide	1.13E-01	3.36E-01	5.07E-04	9.96E-04	1.13E-01	3.37E-01
Iron	1.27E+02	2.60E+02	8.68E+00	6.07E+01	1.36E+02	3.20E+02
Lead	2.37E+01	1.05E+02	2.72E-02	7.15E-02	2.37E+01	1.05E+02
Manganese	2.89E+00	1.39E+01	3.39E-01	2.35E+00	3.23E+00	1.62E+01
Mercury	2.83E-02	7.20E-02	8.78E-05	2.08E-04	2.84E-02	7.22E-02
Nickel	3.56E+01	1.08E+02	1.38E-02	2.32E-02	3.56E+01	1.08E+02
Selenium	2.96E-01	5.42E-01	1.29E-04	1.71E-04	2.96E-01	5.42E-01
Thallium	1.91E-02	4.25E-02	9.46E-05	1.71E-04	1.92E-02	4.27E-02
Vanadium	2.43E+00	4.47E+00	2.31E-03	4.13E-03	2.43E+00	4.47E+00
Zinc	1.31E+02	4.70E+02	7.79E-02	1.41E-01	1.31E+02	4.70E+02

[1] Values from Table E-6.
[2] Values from Table E-7.
[3] Total Exposure Dose = Total Food Dose + Total Water Dose.