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VOLUME III
ORIGINAL

PROGRAM MANAGER FOR
ROCKY MOUNTAIN ARSENAL

U.S. ARMY
MATERIEL COMMAND

— COMMITTED TO PROTECTION OF THE ENVIRONMENT —

FINAL
HUMAN HEALTH EXPOSURE ASSESSMENT
FOR ROCKY MOUNTAIN ARSENAL
VOLUME III
TOXICITY ASSESSMENT
VERSION 4.1
SEPTEMBER 1990
CONTRACT NO. DAAA15-88-D-0024
RIFS2

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13. ABSTRACT (Maximum 200 words)

THE OBJECTIVES OF THE HUMAN HEALTH EXPOSURE ASSESSMENT INCLUDE:

1. ESTIMATE THE TYPE AND MAGNITUDE OF EXPOSURES TO CONTAMINANTS
2. IDENTIFY CONTAMINANTS OF CONCERN
3. IDENTIFY SITES FOR REMEDIAL ACTION
4. RECOMMEND SITES FOR THE NO ACTION REMEDIAL ALTERNATIVE
5. PROVIDE A BASIS FOR DETAILED CHARACTERIZATION OF THE RISK ASSOCIATED WITH ALL SITES.

THIS DOCUMENT CONSISTS OF THE FOLLOWING: AN EXCUTIVE SUMMARY. VOL.I - LAND USE AND EXPOSED POPULATION EVALUATIONS. VOL.II & III - TOXICITY ASSESSMENT (INCLUDES ARMY AND SHELL TOXICITY PROFILES). VOL. IV - PPLV METHODOLOGY. VOL. V - PPLV CALCULATIONS. VOL. VI - STUDY AREA EXPOSURE ANALYSIS (A INTRODUCTION, B WESTERN STUDY AREA, C SOUTHERN STUDY AREA, D NORTHERN CENTRAL STUDY AREA, E CENTRAL STUDY AREA, F EASTERN STUDY AREA, G SOUTH PLANTS STUDY AREA, AND H NORTH PLANTS STUDY AREA. VOL. VII - SUMMARY EXPOSURE ASSESSMENT. VOL. VIII -

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VOLUME III
ORIGINAL

TECHNICAL SUPPORT FOR
ROCKY MOUNTAIN ARSENAL

FINAL
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U.S. ARMY PROGRAM MANAGER'S OFFICE
FOR THE ROCKY MOUNTAIN ARSENAL CONTAMINATION CLEANUP

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LIST OF ACRONYMS

ACGIH	American Council of Governmental Industrial Hygienists
ADI	acceptable daily intake
AIC	acceptable intake chronic
ARL	agency risk level
ASTM	American Society of Testing and Materials
ATSDR	Agency for Toxic Substances and Disease Registry
BCF	bioconcentration factor
BUN	blood urea nitrogen
CAG	Cancer Assessment Group
CAS	Chemical Abstract Service
CIS	Chemical Information System
CNS	central nervous system
DIS	Dialog Information System
D_T	allowable dose
EA	Endangerment Assessment
EC_{50}	effective concentraton
EPA	U.S. Environmental Protection Agency
FDA	Food and Drug Administration
FFA	Federal Facility Agreement
FS	feasibility study
HEAST	Health Effect Assessment Summary Tables
IARC	International Agency for Research on Cancer
IRIS	Integrated Risk Information System; an EPA database
IUPAC	International Union of Pure and Applied Chemistry
H	Henry's Law constant
Koc	soil to water partition coefficient normalized to organic carbon
Kow	octanol/water partition coefficient
LC_{LO}	low inhalation lethal concentration
LC_{50}	lethal concentration$_{50}$; the concentration that was lethal to 50 percent of the test organisms
LD_{LO}	low oral lethal dose
LD_{50}	lethal dose$_{50}$; the dose that was lethal to 50 percent of the test organisms
LOAEL	lowest-observed-adverse-effect level
LOEL	lowest-observed-effect level
MCL	maximum contaminant level in drinking water
MCLG	maximum contaminant level goal (supersedes the term RMCL in current EPA regulatory parlance)
MF	modifying factor
NAS	National Academy of Science
NIOSH	National Institute of Occupational Safety and Health
NOAEL	no-observed-adverse-effect level
NOEL	no-observed-effect level
NTP	National Toxicology Program
OAS	Organizations and the State

LIST OF ACRONYMS (Continued)

OERR	Office of Emergency and Remedial Response
OSHA	Occupational Safety and Health Administration
OWPE	Office of Waste Programs Enforcement
PEL	permissible exposure limit
PPLV	preliminary pollutant limit value
RAGS	Risk Assessment Guidance for Superfund
RfD	reference dose obtained from the EPA IRIS Database
RI	remedial investigation
RMA	Rocky Mountain Arsenal
RMCL	recommended maximum contaminant level developed by EPA for establishing Drinking Water Criteria
RSD	risk-specific dose (based on EPA Carcinogenic Potency Factors)
SGOT	serum glutanic oxalate transaminase
SGPT	serum glutamate pyruvate transaminase
SPHEM	Superfund Public Health Evaluation Manual
STEL	short-term-effect level
TDB	Toxicology Data Bank
TL	tolerance limit
TLV	threshold limit value
TWA	time weighted average
UF	uncertainty factor
USABRDL	U.S. Army Biomedical Research and Development Laboratory
USAMBRDL	U.S. Army Medical Bioengineering Research and Development Laboratory
WHO	World Health Organization

EXECUTIVE SUMMARY

The following report constitutes Volume III of the Rocky Mountain Arsenal (RMA) Exposure Assessment and contains Part II of the Toxicity Assessment for the RMA Target Contaminants (Part I is presented in Volume II of the RMA Exposure Assessment). Sixty-four target contaminants were selected for evaluation based on the criteria set forth in the RMA Chemical Index.

Consistent with the guidance outlined in the Risk Assessment Guidance For Superfund, the objectives of the Toxicity Assessment are first, to summarize the hazards to public and ecological health associated with exposure to contaminants of concern (i.e., development of a toxicity "profile"), and secondly, to identify (or develop if it does not exist) a quantitative index of toxicity for each contaminant (i.e., a reference or risk-specific dose) referred to in this assessment as allowable dose (D_T). These quantitative indices are then used to compute Draft Preliminary Pollutant Limit Values (PPLVs), which are in turn used to evaluate human exposure to contaminants at the Arsenal.

Volumes III and III-A present the toxicological profiles prepared by the Army and Shell for those chemicals beginning with the letters F through Z. Chemicals beginning with the letters A through E are presented in Volumes II and II-A. Note that Shell profiles were not developed for all of the target chemicals.

1.0 INTRODUCTION

One of the components of the Endangerment Assessment (EA) performed for Rocky Mountain Arsenal (RMA) is the Human Health Exposure Assessment. This report is the EA product described by paragraph 24.30 (viii) of the Federal Facility Agreement (FFA). The Human Health Exposure Assessment presents an analysis of the estimated magnitude, frequency, duration, and routes of exposure for predicted future human populations and their associated activities at the Arsenal. The Human Health Exposure Assessment also presents a quantitative framework for establishing risk-based criteria for the protection of human health.

1.1 OBJECTIVES OF THE EXPOSURE ASSESSMENT

The objectives of the Human Health Exposure Assessment are to: (1) estimate the type and magnitude of exposures to the contaminants that are present at specific sites on RMA; (2) identify the contaminants of concern that will be critical to the remediation of specific sites; (3) identify sites within RMA where current contaminant levels in soil and groundwater may pose an unacceptable exposure to projected target populations; (4) provide a first screen of all sites based on preliminary human health risk-based soil criteria to identify which sites are designated as Priority 1 (sites where available soil contaminant concentration data indicate that the maximum detected concentrations exceed the draft human health based criteria), and Priority 2 (sites where available soil contaminant concentration data indicate that the maximum detected concentrations do not exceed the draft human health based criteria); (5) provide a basis for future detailed characterization of risk associated with all sites; and (6) provide the database for establishing a study area-wide and Arsenal-wide perspective of the spatial extent of remediation which may be required at RMA.

1.2 ORGANIZATION OF THE EXPOSURE ASSESSMENT

The above objectives were met by performing a sequence of analyses and evaluations which are documented in eight individual report volumes. The content of these documents is summarized below.

Volume I is an evaluation of land use and exposed populations at RMA which includes: (1) projections of potential land use alternatives and associated human activities for the Arsenal following cleanup; and (2) projections of human populations that may be potentially exposed to residual contamination, following remediation.

Volumes II and III (this report) consist of the Toxicity Assessment of the RMA target contaminants and include: (1) summary toxicity profiles developed by both the Army (Volumes II and III) and Shell (Volumes II-A and III-A) for each target chemical; and (2) a listing of reference doses (RfDs) for noncarcinogens and risk-specific doses (RSDs) for carcinogens, together with a description of the basis for their computation.

Volume IV consists of a detailed presentation of the preliminary pollutant limit value (PPLV) methodology as applied to RMA including a description of the exposure pathway equations together with general parameters appropriate to the projected exposed populations and land uses.

Volume V consists of the second part to the PPLV methodology. It contains: (1) the computed Draft PPLVs for each applicable direct exposure pathway and projected exposed population; (2) supporting chemical-specific parameter data; and (3) a computer user's manual and diskette for computing the Draft PPLVs.

Volume VI (A-H) is a detailed presentation of the study area exposure assessments consisting of comparisons of the site contaminant concentrations measured during the Remedial Investigation (RI) with their corresponding Draft PPLVs, calculated and presented for the range of projected exposed populations and their associated activities.

Volume VII is an integrated presentation of the study area exposure assessments (Volume VI) consisting of: (1) the identification of Arsenal-wide contaminants of concern (i.e., contaminants for which risk characterization will be performed); (2) an Arsenal-wide initial screening to designate sites as Priority 1 and Priority 2; (3) a study area perspective of unacceptable exposure to be used as a first screen in defining remedial boundaries,

along with a comparison to the historical recommendations presented in the 1984 Decontamination Assessment for Land and Facilities at RMA; and (4) the results of an analysis of additivity and consideration of reasonable maximum exposure parameters in the PPLV equations.

Volume VIII is a compilation of the Army's responses to the Organizations and the State (OAS) comments on the Draft Exposure Assessment Report submitted to the parties in July 1989.

APPENDIX B
TOXICITY PROFILES (continued)

APPENDIX B - TOXICITY PROFILES (continued)

1/ Denotes the availability of a Shell profile in Volume III-A.

FLUORIDE[1]

Summary

Small amounts of fluoride in ingested water and beverages have a beneficial effect on the prevention of dental caries, particularly among children. Chronic toxic effects of fluoride exposure include mottling of tooth enamel or dental fluorosis and skeletal fluorosis. Intake of fluoride for long periods in amounts greater than 20-40 mg/day may result in crippling skeletal fluorosis (NAS, 1977). Reported adverse health effects following intake of milligram per liter levels of fluoride in drinking water, including mongolism, cancer, mortality, and mutagenic birth defects, are unconfirmed (NAS, 1977).

Fluoride is commonly found in association with other elements; therefore, the chemical and physical data presented under Chemical and Physical Properties is for a common fluoride compound, sodium fluoride. Physical/chemical data for other fluoride compounds will be different.

CAS Number: 16984-48-8

Chemical Formula: F^-

IUPAC Name: Fluoride

Important Synonyms and Trade Names; Fluoride (1-), Fluoride ion

Chemical and Physical Properties

Molecular Weight: 41.99

Boiling Point: 1,704°C (Merck, 1983)

Melting Point: 993°C (Merck, 1983)

Specific Gravity: 2.78 (Merck, 1983)

Solubility in Water: 4,300 mg/liter at 25°C (Merck, 1983)

Solubility in Organics: Not soluble in alcohol (Merck, 1983)

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[1] Compiled from: United States Army Medical Bioengineering Research and Development Laboratory (USAMBRDL). 1985. Physical/Chemical and Toxicological Data Summaries for 62 Rocky Mountain Arsenal Contaminants. USAMBRDL. Fort Detrick, Frederick, MD.

Also: Berkowitz, J.G., Goyer, M.M., Harris, J.C., Lyman, W.J., Horne, R.A., Nelten, L.H., Harrison, J.E., and Rosenblatt, D.H. 1978. Literature Review--Problem definition studies on selected chemicals. Final Report. Vol. III. Chemistry, toxicology, and potential environmental effects of selected organic pollutants. Contract No. DAMD 17-77-C-7037, Arthur D. Little, Inc. Cambridge, MA (AD BO52946L).

Transport and Fate

Fluorides pass both to and from the atmosphere, hydrosphere, lithosphere, and biosphere in a continuous cycle (Berkowitz et al.,1978). The sources of fluorides are both natural and anthropogenic and include volcanism and entrainment of soil particles by wind and industrial emissions. A majority of these fluorides are transferred back to the earth by wet and dry deposition. In the atmosphere, many inorganic fluoride compounds are hydrolyzed rapidly by water vapor to less volatile compounds. Following reactions with water vapor, anhydrous hydrogen fluoride--an industrial pollutant--yields hydrofluoric acid. Elemental fluorine and halogen fluorides combine with water to form hydrogen fluoride and oxygen (Berkowitz et al., 1978).

Fluoride is commonly found in soils due to its presence as a constituent in a number of abundant minerals. Berkowitz et al. (1978) cite background fluoride levels of 290 ppm in the earth's crust, 715 ppm in igneous rocks, 220 ppm in sandstone, and 560 ppm in shale. A range of 100-300 ppm fluoride is typically found in many soils. A large fraction of natural fluoride in soils is bound to soil particles; however, the amount may vary somewhat with the soils clay content, calcium carbonate content, and pH (Berkowitz et al., 1978--Cite: Gisiger, 1968). Many fluoride-containing minerals do exhibit some degree of water solubility and may be a source of fluoride input to groundwaters. The higher fluoride contents of unpolluted soils found a few feet below the soil surface indicate the mobility of the soluble fractions. In aqueous solution, the predominant form of fluoride is the fluoride ion (F^-), however other forms are possible. In salt water systems (oceans) which contain an average of 1.2-1.4 ppm F^- (Berkowitz et al., 1978) approximately half is in the simple ion form while the majority of the remaining fluoride is in the complex ion form of insoluble magnesium fluoride.

The availability of fluoride for uptake by plants varies with soil conditions. Soil chemistry may also influence the toxicity of fluorides to plants. For example, the availability of fluoride is higher in sandy, acidic, or carbonate rich soils than in clay rich or carbonate poor soils (Berkowitz et al., 1978--Cite: Gisiger, 1968).

Fluorides are easily transferred through most food chains; however, knowledge on the extent of biomagnification is lacking. Berkowitz et al. (1978) summarize fluoride tissue levels for a variety of animals and exposure scenarios. Oysters displayed bioconcentration factors in their soft tissues ranging between 2 and 8 following exposure to increasing fluoride concentrations in seawater for 60 days, while prawns exhibited bioconcentration factors of 356 following exposure to 1.05 ppm F^- in seawater for 72 days.

Health Effects

Humans ingesting water at optimal concentrations of fluoride for the prevention of dental caries do not appear to suffer adverse health effects. Acute fluoride toxicity is rare and usually due to accidental poisoning (Berkowitz et al., 1978). Symptoms include

restlessness, stiffness, anorexia, excessive salivation, nausea, vomiting, abdominal pain, chronic convulsions, depression, and death, usually due to cardiac failure.

Prolonged (chronic) ingestion of elevated levels of fluoride is characterized by dental lesions (i.e., mottling of dental enamel) and skeletal fluorosis. Tooth discoloration can occur at concentrations of fluoride exceeding 2 ppm in water (Berkowitz et al., 1978). Skeletal fluorosis is often asymptomatic until the disease advances to the crippling stage. Symptoms of preskeletal fluorosis include pruritus (severe itching), excessive thirst, severe chronic fatigue, and gastrointestinal upset.

Acutely high doses of sodium fluoride in male rats (50 mg/kg) resulted in an excessive increased urinary excretion of inorganic phosphate, calcium, magnesium, potassium, and sodium (Berkowitz et al., 1978--Cite: Suketa and Mikami, 1977). In other animal studies, male rats injected intraperitoneally with 35 mg/kg sodium fluoride exhibited kidney calcium levels 10 times that of controls and slightly elevated (1.5 times) levels of magnesium (Berkowitz et al., 1978--Cite: Suketa and Mikami, 1977). Dose dependent hyperglycemia was also apparent in these rats.

Effects of fluoride on reproduction in rats and mice have been reported. Female mice raised on 50, 100, or 200 ppm sodium fluoride exhibited retarded growth and impaired reproduction at the two highest doses; half of the animals in the high-dose group died within five weeks. Mice on the low-dose regime showed declines in litter production though other aspects of reproduction were not influenced (Berkowitz et al., 1978--Cite: Messer et al., 1973).

Data on the mutagenicity of fluoride (Mohamed and Chandler, 1976) are inconclusive due to inconsistencies in the experimental protocol. No information on the potential carcinogenicity of inorganic fluorides was located in the available literature.

The acute oral LD_{50} values of sodium fluoride in 30-, 45-, and 90-day-old rats are 54, 52, and 31 mg/kg, respectively. The greater resistance of the 30- and 45-day-old animals may reflect the greater efficiency of the younger skeletal systems in removing fluoride from circulation (Berkowitz et al., 1978).

Toxicity to Wildlife and Domestic Animals

Herbivorous dairy cattle may ingest fluoride through their intake of contaminated forage. Acute fluorine toxicosis in livestock generally occurs with intakes of greater than 250 ppm fluoride (Berkowitz et al., 1978). Symptoms of acute fluoride toxicosis include increased levels of fluoride in the blood and urine, stiffness, anorexia, reduced milk production, excessive salivation, nausea, vomiting, incontinence, chronic convulsions, and cardiac failure. Chronic fluoride toxicosis is characterized by mottled teeth, lameness, and abnormal levels of fluoride in bones and urine (Berkowitz et al.,1978).

Poultry may be more able to tolerate greater levels of fluoride than mammals (Berkowitz et al., 1978). Data on fluoride levels in chickens indicate that growing chicks can tolerate

300 ppm fluoride in their diet, while laying hens can tolerate up to 400 ppm (Berkowitz et al., 1978--Cite: NRC, 1977). Ducks ingesting dietary sodium fluoride at 4,220 ppm exhibited decreased growth but no mortality.

The acute toxicities of fluoride to a variety of fish species are summarized by Berkowitz et al. (1978): Rainbow trout, 5.9-7.5 ppm (LD_{50}) at 7.2°C (softened water); brown trout fry, 15-20 ppm (100 hr LC_{50}) at 12°C (softened water); rainbow trout, 2.7-4.7 ppm (48-240 hr LC_{50}) at 13°C; carp, 75-91 ppm (460 hr LC_{50}) at 20-24°C (softened water) and mosquito fisn, 925 ppm (96-hour LC_{50}).

Regulations and Standards

National Primary Drinking Water Standard (EPA): 4.0 mg/liter (MCL; 40 CFR 141.11)

ACGIH TLV: TWA = 2.5 mg/m^3

OSHA Standards: TWA = 2.5 ppm

Allowable Dose (D_T) Value

The allowable dose (D_T) value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health nor pose a risk of cancer occurrence greater than a predetermined risk level.

For fluoride the D_T value is based on the current EPA reference dose (RfD) (EPA, 1990). The RfD is based on a study of children consuming fluoride in their drinking water at levels ranging from 0-14 ppm (Hodge, 1950). Dental mottling was the effect of concern. A no-observed-adverse-effect level (NOAEL) of 1 mg/liter (1 ppm) was identified from this study. In computing the RfD, EPA assumed a 20 kg bodyweight for children studied between 12 and 14 years of age, and a water consumption rate of 1 liter/day. EPA also assumes that a 20 kg child consumes 0.01 mg/kg/day fluoride in the diet without an adverse effect (EPA, 1990). An uncertainty factor (UF) was not deemed necessary by EPA as the NOAEL is already determined for a sensitive population (i.e., children) and for a length of exposure that encompasses the critical toxic effect (EPA, 1990). Therefore an UF of 1 is used in computing the RfD (D_T). Derivation of the D_T for fluoride includes exposure from both drinking water and dietary exposure and is computed as follows:

$$D_T = \frac{\text{NOAEL (mg/kg/day)}}{\text{UF}} + \text{Dietary Intake}$$

$$= \frac{0.05 + 0.01}{1}$$

$$= 0.05 \text{ mg/kg/day (water)} + 0.01 \text{ mg/kg/day (diet)}$$

$$= 0.06 \text{ mg/kg/day}$$

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FLUOROACETIC ACID[1]

Summary

Fluoroacetic acid and its sodium salt, sodium fluoroacetate are acutely toxic to birds and mammals. Fluoroacetate is used primarily as a rodenticide and is toxic as a result of its oxidative conversion to fluorocitrate in vivo. Fluorocitrate effectively blocks the tricarboxylic acid cycle which is an essential mechanism in mammals for energy production. Data on the environmental persistence of fluoroacetate are lacking.

CAS Number: 144-49-0

Chemical Formula: CH_2FCOOH

IUPAC Name: 2-Fluoroacetic Acid

Important Synonyms and Trade Names: Fluoroethanoic Acid; Gifblaar Poison; MFA; Monofluoroacetic Acid

Chemical and Physical Properties

Molecular Weight: 78.04 (Merck, 1983)

Boiling Point: 165°C (Sax, 1979)

Melting Point: 33°C (Merck, 1983)

Specific Gravity: 1.369 (EPA, 1985)

Solubility in Water: Soluble (Merck, 1983)

Solubility in Organics: Slightly soluble in petroleum ether

Log Octanol/Water Partition Coefficient (Kow): Not Located

Soil to Water Partition Coefficient (Koc): Not Applicable

Bioconcentration Factor: Not Applicable

Vapor Pressure: Not located

Henry's Law Constant: Not Applicable

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[1] Compiled From: Various sources cited in the text and the bibliography.

Transport and Fate

Scant information is available on the transport and fate processes of fluoroacetic acid or its sodium salt, sodium fluoroacetate. Both the acid and the salt are water soluble (EPA, 1985; Gosselin, 1976). Sodium fluoroacetate is also nonvolatile (Gosselin, 1976) and therefore, losses from environmental media due to evaporation would not be expected to occur. Under normal conditions of pH in soil and water it is likely that the compound will be present as a salt rather than as a free acid. Potassium fluoroacetate is a natural toxic constituent of the South African plant Dichaepetalum cymosum (Peters et al., 1981). Fluoroacetate is also a natural constituent of some poisonous plants, notably Acacia georginae, a perennial shrub found in Australia (Gosselin, 1976). Neither plant is likely to occur naturally in the United States.

No data on the stability of fluoroacetic acid (or its sodium salt, sodium fluoracetate) in air, soil, water or its potential for bioaccumulation were located in available literature. However, given the soluble nature of fluoroacetic acid and its sodium salt, bioconcentration would not be expected to occur.

Health Effects

Data presented are for sodium fluoroacetate, the salt of fluoroacetic acid. The fluoroacetate ion itself is not toxic, but is converted in vivo to fluorocitric acid (fluorocitrate), a potent inhibitor of the tricarboxylic acid cycle--an essential mechanism in energy production in mammalian cells (Gosselin, 1976). The block is a result of the inhibition of aconitase that regulates the conversion of citrate to isocitrate. The result is an accumulation of large quantities of citrate in the tissues (Casarett and Doull, 1980). Because the metabolic lesion involves an inhibition of oxidative energy metabolism, the heart and the central nervous system are the critical areas affected (Casarett and Doull, 1980). Symptoms of poisonings include nausea, vomiting, cardiac irregularities, cyanosis, and convulsions. Death is usually the result of ventricular fibrillation or respiratory failure. The estimated lethal dose for humans ranges from 2 to 10 mg/kg (Casarett and Doull, 1980).

Species differences are reported in the types of symptoms which precede death. Dogs usually die of convulsions or respiratory failure; however, in man, monkeys, horses, and rabbits, central nervous system effects are often incidental with the principal complication arising from ventricular fibrillation (Casarett and Doull, 1980).

Few data are available on the effects of chronic poisoning with sodium fluoroacetate; however, renal changes similar to nephrosis have occurred in rats administered acutely lethal or repeated sublethal injections of fluorocitrate (Gosselin, 1976). In one reported case of chronic poisoning, a rabbit exterminator exposed repeatedly over a period of 10 years exhibited severe and progressive lesions of the renal tubular epithelium and milder hepatic neurologic and thyroid dysfunctions (Gosselin, 1976).

No data on reproductive effects, teratogenicity, carcinogenicity, or mutagenicity of fluoroacetic acid or related compounds was located in available literature. The oral LD_{50}

values in rats, mice and guinea pigs are 4.7, 7, and 0.47 mg/kg, respectively (NIOSH, 1983).

Toxicity to Wildlife and Domestic Animals

Some poikilothermic animals are reported to be resistant to fluoroacetate, notably, the South African clawed toad (Xenopus laevis) and some fish such as the bass and the bream (Bauermeister et al., 1977). The intraperitoneal LD_{50} of fluoroacetate in rainbow trout (Salmogairdneri) is 500 umole/kg (Bauermeister et al., 1977).

Acute oral toxicities (LD_{50}) are presented below for a variety of species (Hudson et al., 1984).

Species	LD_{50} (mg/kg)
bullfrogs (Rana catesbeiana)	54.4 mg/kg
mallard ducks (Anas platyrhynchos)	9.11 mg/kg
golden eagles (Aquila chrysaetos)	3.54 mg/kg
California quail (Callipepla californica)	4.63 mg/kg
Japanese quail (Coturnix c. japonica)	12.8 mg/kg
ring-necked pheasant (Phasianus colchicus)	6.46 mg/kg
chukar (Alectoris chukar)	3.51 mg/kg
turkeys (Meleagris gallopavo)	4.76 mg/kg
domestic pigeons (Columba livia)	4.24 mg/kg
house sparrows (Passer domesticus)	3.0 mg/kg
domestic ferrets (Mustela putorius)	1.41 mg/kg
mule deer (Odocoileus h. hemionus)	0.33-1.0 mg/kg

Hudson et al. (1984) reported secondary toxicity in fasted ferrets fed live or dead mice previously dosed with 1, 2, 4, or 8 mg/kg sodium fluoroacetate. Only one ferret survived following the ingestion of one of two low-dose (2 mg/kg) mice.

Regulations and Standards

OSHA PEL: TWA = 0.05 mg/m^3 (sodium salt)

ACGIH TLV: TWA = 0.05 mg/m^3 (sodium salt)
STEL = 0.15 mg/m^3 (sodium salt)

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health nor pose a risk of cancer occurrence greater than a predetermined risk level.

For fluoroacetic acid, the D_T value is derived from an acute oral toxicity value (LD_{50}) in guinea pigs. The D_T is computed as the product of the acute value and an application factor of 1×10^{-5} (Layton et al., 1987). The application factor allows the derivation of an

interim acceptable long-term intake rate (D_T) based on the results of acute tests (LD_{50}) in the absence of more suitable long-term studies (i.e., no-observed-effect level (NOEL) studies). The application factor corresponds to the cumulative percentile on a lognormal distribution of $NOEL/LD_{50}$ ratios for various chemicals. The percentile was chosen to reduce the probability that the calculated dose rate would be above a toxic level; the 5th cumulative percentile was used by Layton et al. (1987) and was found to be equal to 10^{-3}. The application factor also includes a safety factor of 100 to address interspecies and intraspecies variability; therefore, an interim estimate of D_T is obtained when the acute value is multiplied by the application factor. Derivation of this D_T value is as follows:

D_T = Acute oral LD_{50} x Application Factor
= 0.47 mg/kg/day x 1×10^{-5}
= 0.0000047 mg/kg/day

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HEXACHLOROCYCLOPENTADIENE[1]

Summary

Hexachlorocyclopentadiene (HCPD) has not presently been shown to be carcinogenic in animals or humans; however, The National Cancer Institute has selected HCPD for testing. No evidence of mutagenicity has been established for HCPD in either mammalian or bacterial test systems. In animal studies, HCPD given orally resulted in toxic nephrosis in female mice and in male and female rats. Rats exposed to high concentrations of HCPD via inhalation experienced mortality, depressed body weights, increased kidney weights (females only), and pulmonary degenerative changes. HCPD has not resulted in teratogenic or embryotoxic effects following its administration to rabbits and rats; however, maternal toxicity was observed in treated rabbits.

CAS Number: 77-47-4

Chemical Formula: C_5Cl_6

IUPAC Name: 1,2,3,4,5,5-Hexachloro-1,3-cyclopentadiene

Important Synonyms and Trade Names: HCPD; Perchlorocyclopentadiene

Chemical and Physical Properties

Molecular Weight: 273

Melting Point: -9.6°C (EPA, 1984)

Boiling Point: 239°C at 753 mm Hg (Hawley, 1977; Stevens, 1979)
234°C (Irish, 1963)

Specific Gravity: 1.715 at 15.5°C (Hawley, 1977)

Solubility in Organic Solvents: Miscible in hexane (Bell et al., 1978)

Solubility in Water: 2.1 mg/liter at 25°C (Dal Monte and Yu, 1977)
1.8 mg/liter at 28°C (Wolfe et al., 1982)
0.805 mg/liter at 25°C (Lu et al., 1975)
2.1 mg/liter at 25°C (EPA, 1986a)

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[1] Compiled from: USAMBRDL. 1985. Physical/Chemical and Toxicological Summaries for 62 Rocky Mountain Arsenal Contaminants. USAMBRDL. Fort Detrick, Frederick, MD.

Also: U.S. Environmental Protection Agency (EPA) 1984. Health Effects Assessment for Hexachlorocyclopentadiene. Environmental Criteria and Assessment Office, Office of Research and Development. Cincinnati, OH.

Log Octanol/Water Partition Coefficient (Kow): 3.52 (Lyman et al., 1982) Fragment Method
5.04 (Wolfe et al., 1982)

Soil to Water Partition Coefficients (Koc):
13,140 (Lyman et al., 1982) Eqn 4-8 (log Kow = 5.04)
24,330 (Lyman and Loreti, 1987) (log Kow = 5.04)
4,800 (EPA, 1986a)

Bioconcentration Factor:
29 (Veith et al., 1979) (experimental)
11 (EPA, 1980)
279 (Lyman et al., 1982) Eqn 5-2 (log Kow = 3.52)
195 (Davies and Dobbs, 1984) Eqn B (log Kow = 3.52)
107.6 (Davies and Dobbs, 1984) Eqn C (log Kow = 3.52)
179 (Davies and Dobbs, 1984) Eqn A (S = 9)
717 (Davies and Dobbs, 1984) Eqn C (log Kow = 5.04)
1,570 (Davies and Dobbs, 1984) Eqn B (log Kow = 5.04)
3,980 (Lyman et al., 1982) Eqn 5-2 (log Kow = 5.04)

Vapor Pressure: 0.08 mm Hg at 25°C (Irish, 1963)
0.975 mm Hg at 62°C (Stevens, 1979)

Henry's Law Constant: 0.0137 atm-m^3/mole (EPA, 1986a)
5.76 x 10^{-1} Dimensionless
0.027 atm-m^3/mole (Atallah et al., 1980; Wolfe et al., 1982)
1.13 Dimensionless

Transport and Fate

HCPD is known to volatilize rapidly from water (EPA, 1984); however, it is not likely to persist following its release to air. The estimated tropospheric residence time (Cupitt, 1980) is approximately 5 hours based on reactions with hydroxyl radicals and ozone (EPA, 1984). Atmospheric photolysis of HCPD is likely since HCPD has a chromophore which absorbs light in the solar spectrum. The degradation products are thought to be ClCO, diacylchlorides, ketone, and free Cl radical (EPA, 1984).

HCPD is known to photolyze in aqueous media. In flowing bodies of water, photolysis, hydrolysis, volatilization, and biodegradation will all contribute to the loss of HCPD. The photolytic half-life of HCPD in shallow water (<5 cm depth) is estimated to be 10 minutes (EPA, 1984). Hydrolysis is much slower with a half-life ranging from 3-11 days at pHs of 5-9 and temperatures between 25 and 30°C (Wolfe et al., 1982).

The fate and transport of HCPD in soils is affected by its strong tendency to adsorb onto organic matter (EPA, 1984). A range of estimated Kocs is reported above and indicates that sorption of HCPD to soils/sediments and dissolved organic material will occur. The

combined low water solubility and high organic partitioning for HCPD suggests that this compound will not be an environmentally mobile contaminant. HCPD is known to be metabolized by a number of soil microorganisms (EPA, 1984).

A range of estimated and experimental BCFs for HCPD is also reported above. American Society of Testing and Materials (ASTM, 1985) indicates that chemicals with BCFs less than approximately 100 have low potential for causing harm to wildlife and human health via biomagnification of residues up food chains. The magnitude of the estimated concentration factors suggests that appreciable bioconcentration or biomagnification of HCPD residues would occur; however, experimental data appear to indicate that uptake is not considerable (EPA, 1984).

Health Effects

Little data is available on the health effects of HCPD exposures in humans. The compound is very irritating to the eyes and mucous membranes and induces lacrimation, sneezing, and salivation. Repeated contact with the skin causes blistering burns, and inhalation causes pulmonary edema (EPA, 1984).

Subchronic (90-day) oral exposures of mice to doses of HCPD (19, 38, 75, 150, 300 mg/kg) 5 days/week resulted in lesions of the forestomach in both sexes at 38 mg/kg (EPA, 1984). At the highest dose all male mice died by day 8 and 3 females by day 14. In female mice the liver was enlarged, and toxic nephrosis was evident at doses greater than 75 mg/kg. In another phase of the study, rats were orally exposed to doses of 10, 19, 38, 75, and 150 mg/kg HCPD. Mortality and toxic nephrosis was observed in both males and females at doses >38 mg/kg (EPA, 1984). Female rats exposed to 19 mg/kg exhibited lesions of the forestomach. A dose-related depression in bodyweight gain was also observed relative to controls.

Rats and monkeys exposed subchronically (14 weeks) to HCPD via inhalation at doses of 0, 0.1, 0.05, and 0.20 ppm exhibited no treatment-related abnormalities in gross pathology, histopathology, hematology, or clinical chemistry. However, slight but statistically insignificant increases in hemoglobin concentration and erythrocyte counts were seen in the 0.01 and 0.20 ppm male rats and the 0.05 ppm female rats (EPA, 1984).

Male and female rats chronically exposed (30 weeks) via inhalation to doses of 0, 0.05, 0.1, and 0.5 ppm HCPD 6 hours/day, 5 days/week exhibited a number of effects (EPA, 1984). At the highest dose level, mortalities of males and females occurred. Males in this dose group exhibited depressed weight gain following the seventh week of exposure and for the remainder of the study. Females in the medium- and high-dose groups also exhibited depressed body weights. Pulmonary, kidney, and liver degenerative changes were observed in both sexes at the high dose. Kidney weights of high dose females were significantly increased.

No reproductive impairment or evidence of teratogenicity was observed in pregnant rats orally administered HCPD at doses of 3, 10 or 30 mg/kg/day during days 6-15 of gestation

(EPA, 1984). No evidence of teratogenicity was apparent in mice or rabbits orally dosed with 0, 5, 25 or 75 mg/kg/day HCPD during days 6-15 (mice) of gestation (EPA, 1984). Fertility was not significantly different in either dosed mice or rabbits. No maternal toxicity or embryotoxicity occurred in treated mice; however, maternal toxicity did occur at 75 mg/kg/day in rabbits. No embryotoxic effects were noted at any dose level in rabbits (EPA, 1984).

No evidence of the carcinogenicity of HCPD has been demonstrated in animals or humans (EPA, 1984); however, the National Toxicology Program (NTP) was scheduled to start carcinogenicity testing in 1986 (NTP, 1986). It has not been shown to be mutagenic in a variety of bacterial (E. Coli, S. typhinnurium) and mammalian cell cultures (mouselymphoma). The acute oral LC_{50} of HCPD in rats ranges from 500-630 mg/kg (EPA, 1980).

Toxicity to Wildlife and Domestic Animals

Very little information is available on the toxicity of HCPD to wild and domestic animals. The acute oral LD_{50} of HCPD in rabbits ranges between 420 and 620 mg/kg (EPA, 1980). Freshwater and marine aquatic organisms exhibit acute toxic effects at concentrations of HCPD as low as 7 ug/liter, while freshwater organisms exhibit chronic effects at concentrations of 5 ug/liter (EPA, 1986b).

Regulations and Standards

Ambient Water Quality Criteria (EPA, 1986b):

The available data are not adequate for establishing criteria. However, EPA does report the lowest values known to be toxic in aquatic organisms.

Aquatic Life (Freshwater)

Acute Toxicity: 7 ug/liter

Chronic Toxicity: 5.2 ug/liter

Aquatic Life (Saltwater)

Acute Toxicity: 7 ug/liter

Chronic Toxicity: Data are insufficient

Human Health

Criterion: 206 ug/liter

ACGIH TLV: 0.11 mg/m^3

OSHA Standard: TWA = 0.1 mg/m^3

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health nor pose a risk of cancer occurrence greater than a predetermined risk level.

For hexachlorocyclopentadiene, the oral D_T value is based on the current EPA Reference Dose (RfD) (EPA, 1990a). The oral RfD is based on a subchronic oral (gavage) toxicity study in which male and female rats were administered HCPD at doses of 0, 10, 19, 38, 75, or 150 mg/kg/day, 5 days/week for 13 weeks (Abdo et al., 1984). Stomach lesions were observed in 2 of 8 surviving females at 19 mg/kg/day. An increased incidence and severity of effects was noted in both sexes at the higher doses, as well as an increased incidence of nephrotoxicity in females. The NOAEL identified from this study was 7 mg/kg/day. [Note: EPA multiplies the actual NOAEL of 10 mg/kg/day by a conversion factor of 5/7 days to account for the less than continuous exposure duration in determining the final NOAEL level.] An UF of 1,000 is included to address the extrapolation of results to humans (10), intraspecies variability (sensitive subgroups) (10), and to account for the use of a subchronic rather than a chronic experimental exposure (10). Derivation of the D_T value for HCPD is as follows:

$$D_T = \frac{\text{NOAEL (mg/kg/day)}}{\text{UF}}$$

$$= \frac{7}{1{,}000}$$

$$= 0.007 \text{ mg/kg/day}$$

The inhalation D_T for HCPD is also based on an EPA RfD (EPA, 1990b). The RfD is based on a subchronic inhalation study in which rats were exposed to concentrations of 1.67 mg HCPD/m^3 (0.2 mg/kg-day) five days per week over a 13-week period (EPA, 1990b). Though additional details of the study were not provided the toxicological effect of concern involved lesions of the respiratory tract.

An UF of 10,000 is used in the derivation of the RfD to address: 1) interspecies extrapolation, (10); 2) intraspecies variability, (10); 3) extrapolation from a subchronic study (10); and 4) use of a low-observed-adverse-effect-level (LOAEL)(10). Derivation of the inhalation D_T for HCPD is as follows:

$$D_T = \frac{\text{LOAEL (mg/kg/day)}}{\text{UF}}$$

$$= \frac{0.2}{10{,}000}$$

$$= 2 \times 10^{-5} \text{ mg/kg/day}$$

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ISODRIN[1]

Summary

No data on the carcinogenicity, teratogenicity, mutagenicity, chronic toxicity, or reproductive toxicity of Isodrin were located in available literature for animals or humans. The acute oral toxicity of Isodrin in young rats (90 days of age) was 7 mg/kg.

CAS Number: 465-73-6

Chemical Formula: $C_{12}H_8Cl_6$

IUPAC Name: 1,2,3,4,10,10-hexachloro-1,4,4a,5,8,8a-hexahydro-1,4,5,8-endo-endo-dimethanonaphthalene

Important Synonyms and Trade Names: Isodrin; Compound 711

Chemical and Physical Properties

Molecular Weight: 365

Melting Point: 240-242°C (Merck, 1983)

Solubility in Water: 0.16 mg/liter (Lyman et al., 1982) Estimated 1.4 mg/liter; 0.02 mg/liter (Lyman et al., 19__) (Eqn. 2-3 log Kow = 4.38; 6.51)

Log Octanol/Water Partition Coefficient (Kow): 6.51 (Lyman et al., 1982) Fragment Method

Soil to Water Partition Coefficient (Koc):

5,751; 82,880 (Lyman et al., 1982) Eqn 4-8 (log Kow = 4.38; 6.51)
7,448; 339,900 (Lyman and Loreti, 1987) (log Kow = 4.38; 6.51)
8,759; 294,900 (Kadeg et al., 1986) (low Kow = 4.38; 6.51)

Bioconcentration Factor:

11,708 (Davies and Dobbs, 1984) Eqn B (log Kow = 6.5)
51,286 (Lyman et al., 1982) Eqn 5-2 (log Kow = 6.5)

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[1] Compiled from: USAMBRDL. 1985. Physical/Chemical, and Toxicological Summaries for 62 Rocky Mountain Arsenal Contaminants. USAMBRDL. Fort Detrick, Frederick, MD.

Also: Berkowitz, J.G., Goyer, M.M., Harris, J.C., Lyman, W.J.,Horne, R.A., Nelten, L.H., Harrison, J.E., and Rosenblatt, D.H. 1978. Literature Review--Problem definition studies on selected chemicals. Final Report. Vol. II. Chemistry, toxicology, and potential environmental effects of selected organic pollutants. Contract No. DAMD 17-77-C-7037, Arthur D. Little, Inc. Cambridge, MA (ADBO52946L).

4,436 (Davies and Dobbs, 1984) Eqn C (log Kow = 6.5)
1,737 (Davies and Dobbs, 1984) Eqn A (S = .16)
233 (Davies and Dobbs, 1984) Eqn C (log Kow = 4.38)
635 (Davies and Dobbs, 1984) Eqn B (log Kow = 4.38)
1,260 (Lyman et al., 1982) Eqn 5-2 (log Kow = 4.38)

Vapor Pressure: <1 x 10^{-4}mm Hg [estimated for 25°C] (Cogley and Foy, 1978)

Henry's Law Constant: 4.8 x 10^{-4} atm-m3/mole (calculated)
3.4 x 10^{-5} atm-m3/mole (calculated)
1.4 x 10^{-3} Dimensionless
3.2 x 10^{-3} atm-m3/mole (calculated)
1.3 x 10^{-1} Dimensionless

Transport and Fate

Very little information is available on the fate and transport of Isodrin under environmental conditions; indeed, the physical/chemical properties of this compound have not yet been fully characterized. Photodrin formation has been observed following reactions of Isodrin with acid, bromine, hydrogen bromide, and ultraviolet (UV) light in the laboratory (Berkowitz et al., 1978). However, under field conditions, photoconversion of Isodrin to photodrin is not expected, as the maximum UV absorption of Isodrin (198 nm) occurs in a region of the atmosphere where solar radiation is attenuated by both the ozone layer and by water (Berkowitz et al., 1978).

Isodrin is estimated to have a very low vapor pressure and a relatively low solubility in water (Cogley and Foy, 1978). Therefore, it appears reasonable to assume that volatilization of Isodrin to air and leaching of Isodrin-contaminated soil residues to groundwater will not occur to an appreciable extent. A range of Koc is reported above and indicates that sorption of Isodrin to soils/sediments and dissolved organic material will occur. Pavlou (1980) estimates that sorption of chlorinated hydrocarbon pesticides is very high. The combined low estimated water solubility and high organic partitioning indicate that isodrin will exhibit little environmental mobility. The persistence of Isodrin in various soils under varying experimental conditions, as summarized by Berkowitz et al. (1978), indicates that detectable residues may be present in excess of 13 years post-application.

No residues of Isodrin were found in soybeans, corn, or oats grown in soil treated with Isodrin (Nash et al., 1973). Ten weeks following application of Isodrin (0.19 ppm) to soils, up to three percent of the applied quantity was recovered unchanged in the leaves of exposed carrots while 41 percent remained unchanged in the soils (Berkowitz et al., 1978--Cite: Klein et al., 1973). Conversion products which accounted for a majority of the remaining residues were identified as Endrin.

A range of estimated BCFs for Isodrin is also reported above. ASTM (1985) indicates that chemicals with BCFs less than approximately 100 have low potential for causing harm to wildlife and human health via biomagnification of residues up food chains. The magnitude

of the concentration factors suggests that appreciable bioconcentration or biomagnification of Isodrin residues can occur.

Health Effects

No information on the toxicity of Isodrin to humans was located in available literature. Additionally, no data on the carcinogenicity, mutagenicity, subchronic, chronic, or reproductive toxicity were available for animals in the literature reviewed. Only acute oral toxicity data are available for laboratory mice and rats. The LD_{50} values for these animals are 7-15.5 mg/kg for female and male rats (>90 days old); 16.4-27.8 mg/kg for young female and male rats (25-31 days old); and 8.8 mg/kg for mice (Berkowitz et al., 1978).

Toxicity to Wildlife and Domestic Animals

Limited data is available on the toxicity of Isodrin in wild and domestic animals. The dermal LD_{50} in rabbits was estimated at <94 mg/kg (Berkowitz et al., 1978). Endrin, an isomer of Isodrin, was consistently the most toxic chemical among 89 chemicals tested in bobwhite, pheasants, mallards, and Japanese quail (Heath et al., 1972). Isodrin would therefore be expected to exhibit somewhat similar toxic properties.

Comparisons of the toxicities of Isodrin and photodrin in fish to those of several other cyclodiene insecticides indicate that Isodrin was more toxic (Berkowitz et al., 1978). Reported LC_{50} values for freshwater fish were 2.5, 6.0, 6.0, and 1.5 ppb in bass, bluegill, golden shiners, and goldfish, respectively (Berkowitz et al., 1978).

Regulations and Standards

None located.

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health nor pose a risk of cancer occurrence greater than a predetermined risk level.

For Isodrin, the D_T value is derived from an acute oral toxicity value (LD_{50}) in female rats. The D_T is computed as the product of the acute value and an application factor of 1×10^{-5} (Layton et al., 1987). The application factor allows the derivation of an interim acceptable long-term intake rate (D_T) based on the results of acute tests (LD_{50}) in the absence of more suitable long-term studies (i.e., NOEL studies). The application factor corresponds to the cumulative percentile on a lognormal distribution of NOEL/LD_{50} ratios for various chemicals. The percentile was chosen to reduce the probability that the calculated dose rate would be above a toxic level; the 5th cumulative percentile was used by Layton et al. (1987) and was found to be equal to 10^{-3}. The application factor also includes a safety factor of 100 to address interspecies and intraspecies variability; therefore, an interim

estimate of D_T is obtained when the acute value is multiplied by the application factor. Derivation of this D_T value is as follows:

D_T = Acute oral LD_{50} x Application Factor

= 7.0 mg/kg/day x 1×10^{-5}

= 0.00007 mg/kg/day

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ISOPROPYLMETHYLPHOSPHONIC ACID/ISOPROPYL METHYLPHOSPHONATE[1]

Summary

In mice and rats the acute toxicity of sodium isopropylmethylphosphonic acid (IMPA) is low. No data are available on the effects of long-term (chronic) exposures to IMPA in animals or humans. However, a subchronic study in rats indicated that 300 mg/kg was without effect following a 90-day experimental exposure. Sodium IMPA was not mutagenic in tests with Salmonella. No data are available on the carcinogenicity, teratogenicity, or reproductive toxicity of IMPA.

CAS Number: 1832-54-8

Chemical Formula: $C_4H_{10}O_2P$

IUPAC Name: o-Isopropylmethylphosphonic acid

Important Synonyms and Trade Names: Isopropylmethyl phosphonate; IMP; IMPA

Chemical and Physical Properties

Molecular Weight: 140

Solubility in Water: 48 g/liter (estimated) (Lyman et al., 1982)

Specific Gravity: 1.109 (Rosenblatt et al., 1975)

Log Octanol/Water Partition Coefficient (Kow): -0.54 (Small, 1984)

Soil to Water Partition Coefficient (Koc): Not Applicable

Bioconcentration Factor: Not Applicable

Vapor Pressure: Not Located

Henry's Law Constant: Not Applicable

Transport and Fate

Scant data are available on the transport and fate processes for IMPA/IMP in environmental media. The form which is likely to occur in the environment (free acid or salt) will be governed by ambient pH conditions. The pKa value for IMPA is well below

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[1] Compiled from: Various referenced sources.

Also: Note that both names refer to the same compound. The form encountered in the environment will be dependent on ambient pH conditions.

the normal range of pHs typical of soil or water (Small, 1984). Therefore, it is likely that the predominant form will be a salt with cations such as Na^{+}, Ca^{++}, and Al^{+++} (Small, 1984). The estimated vapor pressure indicates the potential for some volatilization; however, in moist soils or water, the solubility of IMPA would probably tend to offset volatilization. IMPA appears to be fairly resistant to hydrolysis. In a study by Howells et al. (1973) no hydrolysis of IMPA to methylphosphonic acid (a principal hydrolysis product) was observed after several months in a hydroponic solution.

In a study by Cook et al. (1978), IMPA was utilized by selected strains of sewage bacteria as a phosphorus source. Daughton et al. (1979) found IMPA to be less bound than methyl phosphoric acid to spodosol, a soil with high binding affinity for inorganic orthophosphate. Little sorption of IMPA to soils is expected to occur given its high water solubility. The combined low organic partitioning behavior and high water solubility suggest that IMPA will be a mobile contaminant.

Bioconcentration data for IMPA/IMP were not located in available literature. However, given the high aqueous solubility and low organic partitioning, bioconcentration would not be expected to occur.

No data on the persistence of IMPA in air, soil, or water was located in available literature.

Health Effects

Mecler (1981) has evaluated the mammalian toxicity of sodium IMPA. No signs of irritation were observed following ocular administration of sodium IMPA in rabbits. Similarly, no signs of systemic toxicity were noted following application of sodium IMPA (2.0 g/kg) to intact and abraded rabbit skin; however, mild skin irritation was evident (Mecler, 1981). Sodium IMPA (0.1 percent solution) did not induce dermal sensitization in guinea pigs injected intradermally over a three-week period (Mecler, 1981).

In a subchronic toxicity test with sodium IMPA, rats were administered the compound in their drinking water at concentrations of 300, 1,000, or 3,000 ppm for a period of 90 days (Mecler, 1981). No changes in body weight, food intake, water intake, clinical chemistry, or hematological parameters were seen in treated rats compared to controls (Mecler, 1981). The highest identified NOEL was 3,000 ppm (300 mg/kg). Sodium IMPA did not exert a mutagenic effect in any of five Salmonella strains in the Ames Assay when tested with or without liver activation (Mecler, 1981). No data on reproductive toxicity, teratogenicity, chronic toxicity, or carcinogenicity were located in available literature.

The oral LD_{50} values of sodium IMPA in male and female rats are 7,650 mg/kg and 6,070 mg/kg, respectively (Mecler, 1981). In mice, the LD_{50} values are 5,620 and 6,550 mg/kg in male and female mice, respectively (Mecler, 1981).

Toxicity to Wildlife and Domestic Animals

No data on the toxicity of IMPA to wildlife or domestic animals were located in available literature.

Regulations and Standards

None located.

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health nor pose a risk of cancer occurrence greater than a predetermined risk level.

For IMPA, the D_T value is based on the results of a subchronic (90-day) toxicity study utilizing rats (Mecler, 1981). In this study, rats were administered concentrations of sodium IMPA (300, 1,000, and 3,000 ppm) in drinking water. Parameters monitored in the study included bodyweight, food intake, water intake, clinical chemistry, and hematology. No effects on any of these parameters were observed at any treatment level and therefore the highest NOEL identified from the study was 3,000 ppm (300 mg/kg/day). An UF of 1,000 is included in the derivation of the D_T to address the extrapolation of results to humans (10), intraspecies variability (sensitive subgroups) (10), and to account for the use of a subchronic rather than a chronic exposure duration (10). Derivation of the D_T for IMPA is as follows:

$$D_T = \frac{\text{NOEL}}{\text{UF}} \text{ (mg/kg/day)}$$

$$= \frac{300}{1{,}000}$$

$$= 0.30 \text{ mg/kg/day}$$

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LEAD[1]

Summary

Lead is a heavy metal that exists in one of three oxidation states, 0, +2, and +4. There is suggestive evidence that some lead salts are carcinogenic, inducing kidney tumors in mice and rats. Lead is also a reproductive hazard, and it can adversely affect the brain and central nervous system by causing encephalopathy and peripheral neuropathy. Chronic exposure to low levels of lead can cause subtle learning disabilities in children. Exposure to lead can also cause kidney damage and anemia and may have adverse effects on the immune system.

CAS Number: 7439-92-1

Chemical Formula: Pb

IUPAC Name: Lead

Chemical and Physical Properties

Atomic Weight: 207.19

Boiling Point: 1,740°C

Melting Point: 327.5°C

Specific Gravity: 11.35 at 20°C (liquid)

Vapor Pressure: 1.77 mm Hg at 1,000°C (Merck, 1983)

Solubility in Water: Insoluble; some organic compounds are soluble

Solubility in Organics: Soluble in HNO_3 and hot, concentrated H_2SO_4

Transport and Fate

Some industrially produced lead compounds are readily soluble in water (EPA, 1979). However, metallic lead and the common lead minerals are insoluble in water. Natural compounds of lead are not usually mobile in normal surface or groundwater because the

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[1] Compiled from: U.S. Environmental Protection Agency, Office of Waste Program Enforcement. September 1985. Chemical, physical, and biological properties of compounds present at hazardous waste sites. A Final Report Prepared by Clement Associates, Inc., Arlington, Virginia.

Also: USAMBRDL. 1985. Physical/Chemical and Toxicological Summaries for 62 Rocky Mountain Arsenal Contaminants. USAMBRDL. Fort Detrick, Frederick, MD.

lead leached from ores is absorbed by ferric hydroxide or combines with carbonate or sulfate ions to form insoluble compounds.

Movement of lead and its inorganic and organolead compounds as particulates in the atmosphere is a major environmental transport process. Lead carried in the atmosphere can be removed by either wet or dry deposition. Although little evidence is available concerning the photolysis of lead compounds in natural waters, photolysis in the atmosphere occurs readily. These atmospheric processes are important in determining the form of lead entering aquatic and terrestrial systems.

The transport of lead in the aquatic environment is influenced by the speciation of the ion. Lead exists mainly as the divalent cation in most unpolluted waters and becomes adsorbed into particulate phases. However, in polluted waters, organic complexation is most important. Volatilization of lead compounds probably is not important in most aquatic environments.

Sorption processes appear to exert a dominant effect on the distribution of lead in the environment. Adsorption to inorganic solids, organic materials, and hydrous iron and manganese oxides usually controls the mobility of lead and results in a strong partitioning of lead to soils and the bed sediments in aquatic systems. The sorption mechanism most important in a particular system varies with geological setting, pH, Eh, availability of ligands, dissolved and particulate ion concentrations, salinity, and chemical composition. The equilibrium solubility of lead with carbonate, sulfate, and sulfide is low. Over most of the normal pH range, lead carbonate, and lead sulfate control solubility of lead in aerobic conditions, and lead sulfide and the metal control solubility in anaerobic conditions.

Lead in soil is not easily taken up by plants, and therefore its availability to terrestrial organisms is somewhat limited. Biomethylation of lead by microorganisms can remobilize lead to the environment. Bioaccumulation of lead has been demonstrated for a variety of organisms. BCFs in freshwater organisms range from 42 to 1,700 for four invertebrate and two fish species (EPA, 1986a). In saltwater organisms, available BCFs range from 17 to 2,600 (EPA, 1986a). Microcosm studies indicate that lead is not biomagnified through the food chain.

Health Effects

There is evidence that several lead salts are carcinogenic in mice or rats, causing tumors of the kidneys following oral or parenteral administration. Data concerning the carcinogenicity of lead in humans are inconclusive. The available data are not sufficient to evaluate the carcinogenicity of organic lead compounds or metallic lead. Lead has been classified according to EPA's Guidelines for Carcinogenic Risk Assessment in EPA's Group B2 (sufficient evidence in animals) based upon the evidence of kidney tumors in rats following oral administration and inadequate evidence in humans (50 Federal Register 46971, Wed. Nov. 13, 1985).

There is equivocal evidence that exposure to lead causes genotoxicity in humans and animals. The available evidence indicates that lead presents a hazard to reproduction and exerts a toxic effect on conception, pregnancy, and the fetus in humans and experimental animals (EPA, 1977; EPA, 1980).

Many lead compounds are sufficiently soluble in body fluids to be toxic (EPA, 1977; EPA, 1980). Exposure of humans or experimental animals to lead can result in toxic effects in the brain and central nervous system, the peripheral nervous system, the kidneys, and the hematopoietic system. The metabolism and retention of lead (primarily in bone) has been well studied. Chronic exposure to inorganic lead by ingestion or inhalation can cause lead encephalopathy, and severe cases can result in permanent brain damage. Lead poisoning may cause peripheral neuropathy both in adults and children. Permanent learning disabilities in children that are clinically undetectable may be caused by exposure to relatively low levels of lead. Short-term exposure to lead can cause reversible kidney damage; however, prolonged exposure at high concentrations may result in progressive kidney damage and kidney failure. Anemia, due to inhibition of hemoglobin synthesis and a reduction in the life span of circulating red blood cells, is an early manifestation of lead poisoning. Several studies with experimental animals suggest that lead may interfere with various aspects of the immune response.

Young children are deemed a high risk group for lead exposure for a number of reasons: 1) their dietary intake in mg/kg body weight is higher than that of adults; 2) young children tend to ingest greater quantities of dirt than do adults (and such soil, particularly in urban areas, can be highly contaminated); and 3) some young children have a pica habit and may consume old, lead-based paint peelings.

Toxicity to Wildlife and Domestic Animals

Freshwater vertebrates and invertebrates are more sensitive to lead in soft water than in hard water (EPA, 1980; EPA, 1983). At a hardness of about 50 mg/liter $CaCO_3$, the median effect concentrations for nine families range from 140 to 236,000 ug/liter. Chronic values for Daphnia magna and the rainbow trout are 12.26 and 83.08 ug/liter, respectively, at a hardness of about 50 mg/liter. Acute-chronic ratios calculated for three freshwater species ranged from 18 to 62. Freshwater algae show an inhibition of growth at concentrations above 500 ug/liter.

Acute values for twelve saltwater species range from 476 ug/liter for the common mussel to 27,000 ug/liter for the soft shell clam. The acute-chronic ratio for this species is 118. Reported BCFs range from 17.5 for the quahog clam to 2,570 for the blue mussel. Saltwater algae are adversely affected at lead concentrations as low as 15.8 ug/liter.

Lead is known to occur in the tissue of many free-living wild animals, including birds, mammals, fishes, and invertebrates. Reports of avian poisoning usually involve waterfowl ingesting spent lead shot with grit pebbles which they swallow to aid in digestion. Typical signs of avian lead poisoning include regurgitation, tremors, wing-droop, slowness and reluctance to move, and anorexia (Hudson et al., 1984). There is some evidence that lead,

at concentrations occasionally found near roadsides and smelters, can eliminate or reduce populations of bacteria and fungi on leaf surfaces and in soil. Many of these microorganisms play key roles in the decomposer food chain.

Cases of lead poisoning have been reported for a variety of domestic animals, including cattle, horses, dogs, and cats. Several types of anthropogenic sources are cited as the source of lead in these reports. Because of their indiscriminate eating habits, cattle often experience the greatest incidence of lead toxicity among domestic animals.

Regulations and Standards

Ambient Water Quality Criteria (EPA, 1986a):

The concentrations below are for active lead, which is defined as the lead that passes through a 0.45-um membrane filter after the sample is acidified to pH 4 with nitric acid.

Aquatic Life (Freshwater)

Acute toxicity: $e^{[1.34\ (\ln(\text{hardness})) - 2.014]}$ug/liter

Chronic toxicity: $e^{[1.34\ (\ln(\text{hardness})) - 5.245]}$ug/liter

At hardness of 50, 100, and 200 mg/l $CaCO_3$ the acute criteria are 34, 82, and 200 ug/l.

At hardness of 50, 100, and 200 mg/l $CaCO_3$ the chronic criteria are 1.3, 3.2, and 7.7 ug/l.

Aquatic Life (Saltwater)

Acute toxicity: 140 ug/liter

Chronic toxicity: 5.6 ug/liter

Human Health

Criterion: 50 ug/liter

National Primary Drinking Water Standard (EPA): 50 ug/liter

ACGIH TLV: TWA = 0.15 mg/m^3 (inorganic dusts and fumes)

NIOSH Recommended Standard: TWA = 0.10 mg/m^3 (inorganic lead)

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health nor pose a risk of cancer occurrence greater than a predetermined risk level.

For lead, the oral and inhalation D_T values are based on Acceptable Intake Chronic (AIC) estimates reported in the Superfund Public Health Evaluation Manual (EPA, 1986b). These are 1.4×10^{-3} mg/kg/day for oral exposures, and 4.3×10^{-4} mg/kg/day for inhalation. Details of the underlying studies were not available nor was information on the type of UF(s) incorporated in the intake estimates. The EPA is currently evaluating the available data to derive RfDs for lead; however, these are not expected until sometime in 1990 (EPA, 1986c).

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LEWISITE/LEWISITE OXIDE[1]

Summary

Lewisite is an arsenic-containing compound formerly manufactured as a chemical warfare agent. Lewisite oxide is the hydrolysis product of Lewisite. Both are vesicants (blister agents) and highly toxic. The acute oral LD_{50} in rats for Lewisite oxide is 5 mg/kg. In humans, inhalation of 6 ppm Lewisite for 30 minutes is lethal. There is evidence linking lewisite exposure and the development of certain cancers in humans.

CAS Numbers: 541-25-3 (Lewisite)
333-25-5 (Lewisite oxide)

Chemical Formula: $C_2H_2AsCl_3$ (Lewisite)
C_2H_2AsClO (Lewisite oxide)

IUPAC Name: Dichloro-(2-chlorovinyl)arsine (Lewisite)
Dichloro-(2-chlorovinyl)arsine oxide (Lewisite oxide)

Important Synonyms and Trade Names: Lewisite; Lewisite oxide

Chemical and Physical Properties

Molecular Weights: 207 (Lewisite) (Merck, 1983)
153 (Lewisite oxide) (USAMBRDL, 1985)

Melting Point: 0.1°C (Merck, 1983)

Boiling Point: 190°C (Merck, 1983)

Specific Gravity: 1.88 (Merck, 1983)

Solubility in Water: Insoluble (Merck, 1983)

Solubility in Organics: Soluble in most organic solvents (Merck, 1983)

Vapor Pressure: 0.395 mm Hg at 20°C (Merck, 1983)
0.58 mm Hg at 25°C (DA, 1974)

Vapor Density: 7.1 (EPA, 1985)

[1] Compiled from: USAMBRDL. 1985. Physical/Chemical and Toxicological Summaries for 62 Rocky Mountain Arsenal Contaminants. USAMBRDL. Fort Detrick, Frederick, MD.

Transport and Fate

Very little data are available on the fate or transport of Lewisite and Lewisite oxide in environmental media. In aqueous solution, Lewisite or the oxide is easily oxidized to 2-chlorovinyl-arsenic acid by a variety of oxidants (Rosenblatt et al., 1975). Lewisite is also rapidly hydrolyzed to Lewisite oxide. The latter may further combine with water to form a geminal diol which is slightly acidic. No information is available on the transport of Lewisite/Lewisite oxide via volatilization; however, the vapor pressure of Lewisite indicates the potential for some volatility. Interactions of Lewisite with airborne water vapors could result in hydrolysis to Lewisite oxide.

In soil, it is thought that Lewisite behaves in a manner analogous to sodium arsenite and is oxidized presumably by microorganisms (Rosenblatt et al., 1975). Oxidation of Lewisite or its oxide to the less toxic form--2-chlorovinyl-arsenic acid is slow (Rosenblatt et al., 1975). No data on the uptake of either compound in plants or aquatic biota was located in available literature. However, because of its extreme phytotoxicity it would appear that the potential for bioconcentration of Lewisite oxide through the food chain is not likely (Rosenblatt et al., 1975).

Health Effects

Lewisite is a potent vesicant and is highly toxic by all routes of exposure. The low lethal dose in humans is 6 ppm via inhalation for a 30 minute exposure. As little as 2 ml of Lewisite via dermal exposure can be fatal (Merck, 1983). Eye lesions can be incurred at concentrations of 20 mg/m^3 (DA, 1974). Signs and symptoms of exposure include pulmonary edema, diarrhea, restlessness, weakness, subnormal temperature, and low blood pressure. Ocular contact results in an immediate searing sensation with permanent loss of sight if decontamination is not immediate. Dermal contact results in stinging sensations and reddening, usually within 30 minutes. Blistering follows and usually occurs within 12 hours of contact (EPA, 1985).

No data on the chronic toxicity, reproductive toxicity, teratogenicity, or mutagenicity of Lewisite/Lewisite oxide was located. Nishimoto et al. (1986), Shigenobu (1980), and Yamada (1963) report that retired workers formerly involved in the production of poison gases (Mustard, Lewisite, and others) have a high risk of various types of malignant tumors, including cancers of the respiratory tract. However, problems associated with multiple chemical exposures of these workers precludes definitive statements of the carcinogenic potential of Lewisite. Krause and Grussendorf (1979) and Krause and Grussendorf (1978) report cases of Bowen's Disease (development of intraepidermal carcinoma) in two people following a past dermal exposure to Lewisite. In both cases a tumor relapse occurred following an initial surgical removal of the cancerous tissue.

In rats, the acute dermal and subcutaneous LD_{50} values for Lewisite are 24 and 1 mg/kg, respectively (NIOSH, 1982); the inhalation LC_{50} for mice is 150 mg/m^3 (10 minute exposure). The oral LD_{50} for Lewisite oxide in rats is 5 mg/kg (NIOSH, 1982). Dermal and subcutaneous LD_{50} values for Lewisite in guinea pigs are 12 and 1 mg/kg, respectively

(NIOSH, 1982). In rabbits, the oral and intravenous LD_{50} values for Lewisite oxide are 3 and 1 mg/kg. The oral and subcutaneous LD_{50} values for Lewisite oxide in the guinea pig are 2 and 0.2 mg/kg (NIOSH, 1982).

Toxicity to Wildlife and Domestic Animals

Little data are available on the toxicity of Lewisite/Lewisite oxide to wild or domestic animals. The dermal and subcutaneous LD_{50} values for Lewisite in dogs are 15 and 2 mg/kg, respectively (NIOSH, 1982). In rabbits, the dermal, subcutaneous, and intravenous LD_{50} values for Lewisite are 6, 2, and 0.5 mg/kg, respectively (NIOSH, 1982).

Regulations and Standards

OSHA TLV: TWA = 0.5 mg/m^3 (as As for Lewisite)
TWA = 0.5 mg/m^3 (as As for Lewisite oxide)

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health nor pose a risk of cancer occurrence greater than a predetermined risk level.

For Lewisite/Lewisite oxide, the D_T value is derived from an acute oral toxicity value (LD_{50}) for Lewisite oxide in guinea pigs. The D_T is computed as the product of the acute value and an application factor of 1×10^{-5} (Layton et al., 1987). The application factor allows the derivation of an interim acceptable long-term intake rate (D_T) based on the results of acute tests (LD_{50}) in the absence of more suitable long-term studies (i.e. NOEL studies). The application factor corresponds to the cumulative percentile on a lognormal distribution of NOEL/LD_{50} ratios for various chemicals. The percentile was chosen to reduce the probability that the calculated dose rate would be above a toxic level; the 5th cumulative percentile was used by Layton et al. (1987) and was found to be equal to 10^{-3}. The application factor also includes a safety factor of 100 to address interspecies and intraspecies variability; therefore, an interim estimate of D_T is obtained when the acute value is multiplied by the application factor. Derivation of this D_T value is as follows:

D_T = Acute oral LD_{50} x Application Factor
= 2 mg/kg/day x 1×10^{-5}
= 0.00002 mg/kg/day

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MALATHION[1]

Summary

Malathion is a member of the organophosphorous class of pesticides. Its primary mode of toxicity (acute and chronic exposures) is via the inhibition of the enzyme acetycholinesterase in peripheral and central nervous systems. Chronic exposure to high levels of Malathion in rats resulted in reduced food intake and reduced weight gain. Effects on reproductive parameters were observed in rats fed diets containing 4,000 ppm Malathion. Both positive and negative results have been obtained in mutagenicity tests utilizing bacterial and mammalian test systems. No evidence of carcinogenicity has been observed in several studies utilizing rats and mice.

CAS Number: 121-75-5

Chemical Formula: $C_{10}H_{19}PO_6S_2$

IUPAC Name: S-(1,2-dicarbethoxyethyl)0,0-dimeth; dithiophosphate

Important Synonyms and Trade Names: Malathion

Chemical and Physical Properties

Molecular Weight: 330 (Merck, 1983)

Boiling Point: 156°C at 0.7 mm Hg (Merck, 1983)

Melting Point: 2.9°C (Merck, 1983)

Specific Gravity: 1.2315 at 25°C (Merck, 1983)

Solubility in Water: 145 mg/liter (Merck, 1983)

Solubility in Organics: Miscible with numerous organic solvents

Log Octanol/Water Partition Coefficient (Kow):
2.89 (Hansch and Leo, 1979)
2.36; 2.89 (Rao and Davidson, 1983)
2.89 (EPA, 1986a)

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[1] Compiled from: USAMBRDL, 1985. Physical/Chemical and Toxicological Summaries for 62 Rocky Mountain Arsenal Contaminants. USAMBRDL. Fort Detrick, Frederick, MD.

Also: National Academy of Science (NAS). 1977. Drinking Water and Health. Volume I. National Academy of Sciences, Washington,DC. pg. 620-626.

Soil to Water Partition Coefficient (Koc):
1,797 (Rao and Davidson, 1983) Table 1 (Mean of 20 soils)

Bioconcentration Factor:
37.3 (Davies and Dobbs, 1984) Eqn A (S = 145)
92.6 (Lyman et al., 1982) Eqn 5-2 (log Kow = 2.89)
49 (Davies and Dobbs, 1984) Eqn C (log Kow = 2.89)
82 (Davies and Dobbs, 1984) Eqn B (log Kow = 2.89)

Vapor Pressure: 4×10^{-5} mm Hg at 30°C (Merck, 1983)
2.4×10^{-5} mm Hg at 25°C (Lyman et al., 1982) Estimated

Henry's Law Constant: 7.2×10^{-8} atm-m^3/mole (calculated)
9×10^{-8} atm-m^3/mole (calculated)
1.2×10^{-7} atm-m^3/mole (calculated)
5.0×10^{-6} Dimensionless

Transport and Fate

The somewhat low vapor pressure indicates that volatilization is not a major transport process for Malathion from environmental media, however, it may be enhanced by covaporization with water. The stability of Malathion in aqueous solution is pH dependent (NAS, 1977). At a pH of 9, the half-life of Malathion is 12 hours; it is hydrolyzed in a matter of minutes at a more alkaline pH of 12. At more acidic pH values of 5-7, essentially no hydrolysis occurs (NAS, 1977). The half-life of Malathion in raw river water is reported to be less than one week; in distilled water it is stable up to three weeks (NAS, 1977). It is thought that the differences in residence time are a function of biological activity. NAS (1977) summarizes data in which Malathion introduced into collected water samples at concentrations of 10 mg/liter was degraded almost completely after 10 days. In general, Malathion is degraded in water more rapidly than other organophosphorous compounds under similar conditions (NAS, 1977).

A range of estimated Kocs is reported above and indicates that sorption of Malathion to soils/sediments and dissolved organic material will occur. Pavlou (1980) estimates that sorption of organophosphorous insecticides will range from low to moderate. The combined water solubility and organic partitioning of Malathion suggest that this compound will exhibit some degree of environmental mobility.

A range of estimated BCFs for Malathion is also reported above. ASTM (1985) indicates that chemicals with BCFS less than approximately 100 have low potential for causing harm to wildlife and human health via biomagnification of residues up food chains. The magnitude of the concentration factors suggests that appreciable bioconcentration or biomagnification of Malathion residues is not likely to occur.

Health Effects

The primary health effect stemming from exposure to organophosphorous compounds like Malathion, is through inhibition of the enzyme acetylcholinesterase. Inhibition is increased as a result of the oxidative conversion of Malathion to malaoxon in vivo, a more potent inhibitor of acetylcholinesterase (Casarett and Doull, 1980). In humans, severe exposure to organophosphates can result in respiratory failure due to paralysis of the respiratory muscles, bronchoconstriction and bronchial secretion, and depression of the respiratory center in the brain (Casarett and Doull, 1986).

Chronic feeding studies (2 years) with Malathion at dosages of 100, 1,000, and 5,000 ppm resulted in no gross effects in rats at the 100 and 1,000 ppm dosages (NAS, 1977--Cite: Hazleton and Holland, 1953). At 5,000 ppm, food intake and weight gain were reduced. Significant decreases in plasma, erythrocyte, and brain cholinesterase activity occurred in the two high dose groups. In another chronic feeding study, dosages of 500, 5,000, and 20,000 ppm in the diet of rats resulted in significant inhibition of erythrocyte cholinesterase activity at all dosages. Reduced growth and food intake were observed in the highest dose group (NAS, 1977--Cite: Golz and Shaffer, 1956). Subacute toxicity studies with dosages ranging from 100 to 5,000 ppm also revealed no effect on food intake, weight gain or growth, but significant decreases in cholinesterase activity were observed at the higher dosages.

Reproductive effects have been observed in rats fed diets containing 4,000 ppm Malathion. The number of newborn rats alive at one week was 105 for controls and 56 for treated animals. Only 34 treated animals survived to weaning at age 21 days, compared with 75 controls. Average body weights of treatment animals were significantly lower than control body weights (NAS, 1977--Cite: Kalow and Marton, 1961).

Malathion has yielded positive results for mutagenicity in tests with numerous bacterial and mammalian test systems including: E. Coli K12, Salmonella (activated), Chinese hamster fibroblasts, Chinese hamster V79 cells, mouse primary spermatocyte, and rat bone marrow cells (NIOSH, 1982). Significant (positive) results were also obtained following a mutagenicity test with human fetal lung fibroblasts (NIOSH, 1982). No evidence of carcinogenicity has been observed in several studies with mice and rats.

The low oral lethal dose of Malathion in humans ranges between 246 and 857 mg/kg. The acute oral LD_{50} in rats and mice are 370 and 770 mg/kg, respectively (NIOSH, 1982).

Toxicity to Wildlife and Domestic Animals

Salmonids and centrarchids appear to be the freshwater fish most sensitive to Malathion. Many aquatic invertebrates appear to be more sensitive than fish to Malathion (EPA, 1986b). The 96-hour LC_{50} ranges between 101 and 285 ug/liter for three centrarchid and three salmonid species (EPA, 1986a). The 96-hour LC_{50} for the rainbow trout (Salmo

gairdneri) is 68 ug/liter and 50 ug/liter in the largemouth bass (Micropterus salmoides). The 96-hour LC_{50} for the invertebrate Gammarus lacustris is reported to be 1.0 ug/liter.

The acute oral LD_{50} values of Malathion in mallard ducks, pheasants, and songbirds are 1,485 mg/kg, 167 mg/kg and 403 mg/kg, respectively (Hudson et al., 1984). The range in values illustrates the species sensitivity. The acute intraperitoneal LD_{50} in dogs is 1,857 mg/kg and 550 mg/kg in guinea pigs. The acute oral and dermal LD_{50} values for rabbits are 250-1,200 and 4,100 mg/kg, respectively, and in guinea pigs, 570 and 6,700 mg/kg, respectively (USAMBRDL, 1985).

Regulations and Standards

Ambient Water Quality Criteria (EPA, 1986b):

Aquatic Life (Freshwater):

Acute Toxicity: Data are inadequate

Chronic Toxicity: 0.01 ug/liter

Aquatic Life (Saltwater):

Acute Toxicity: Data are inadequate

Chronic Toxicity: 0.01 ug/liter

Human Health:

No criterion has been established.

ACGIH TLV: TWA = 10 mg/m^3 (skin)

OSHA PEL: TWA = 10 mg/m^3 (total dust)
5 mg/m^3 (respirable)

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health nor pose a risk of cancer occurrence greater than a predetermined risk level.

For Malathion, the oral D_T value is based on the current EPA RfD (EPA, 1990). The RfD is based on a subchronic oral toxicity study in human volunteers (male) (Moeller and Rider, 1962). The groups of healthy male volunteers were administered Malathion in capsule doses of 8 mg/day for 32 days, 16 mg/day for 47 days, or 24 mg/day for 56 days. Cholinesterase activity was determined before, during, and after administration of the

cholinesterase activity. The NOEL identified from this study was 16 mg/day (0.23 mg/kg/day assuming a 70 kg reference human weight). An UF of 10 was employed to address intraspecies variability (sensitive subgroups) (10). Derivation of the D_T value for Malathion is as follows:

$$D_T = \frac{\text{NOEL mg/kg/day}}{\text{UF}}$$

$$= \frac{0.23}{10}$$

$$= 0.023 \text{ mg/kg/day}$$ [Note: EPA rounds this number to 0.02 in their derivation.]

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MERCURY (INORGANIC)[1]

Summary

Inorganic mercury is reported to be teratogenic and embryotoxic in studies with experimental animals. In humans, prenatal exposure to mercury vapors has been associated with spontaneous abortions and infant mortalities. The major target organs for inorganic mercury compounds are the central nervous system and the kidneys. Mutagenic responses in mammalian cell cultures have been equivocal.

CAS Number: 7439-97-6

Chemical Formula: Hg

IUPAC Name: Mercury

Chemical and Physical Properties

Atomic Weight: 200.59 (Merck, 1983)

Boiling Point: 356.72°C (Merck, 1983)

Melting Point: -38.87°C (Merck, 1983)

Specific Gravity: 13.534 (Merck, 1983)

Solubility in Water: 56.2 ug/liter at 25°C (Merck, 1983)

Solubility in Organics: Depends on chemical species

Vapor Pressure: 0.0012 mm Hg at 20°C (EPA, 1984a)
0.002 mm Hg at 25°C (Merck, 1983)

Transport and Fate

Inorganic mercury can exist in three oxidative states in the environment, including metallic (Hg°), mercurous (Hg_2^{++}), and mercuric(Hg^{++}). In general, the mercurous salts are much less soluble than the more commonly found mercuric salts. The nature and solubility of the chemical species that occur in an environmental system will depend on the redox potential and the pH of the environment.

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[1] Compiled from: U.S. Environmental Protection Agency, Office of Waste Program Enforcement. September 1985. Chemical, physical,and biological properties of compounds present at hazardous waste sites. A Final Report Prepared by Clement Associates, Inc., Arlington, Virginia.

Also: U.S. Environmental Protection Agency (EPA). 1984a Mercury Health Effects Update. Health Issue Assessment. Final Report. Office of Health and Environmental Assessment. Washington, D.C. EPA-600/8-84-019F.

Mercury can volatilize to the atmosphere from aquatic and terrestrial sources. Volatilization is reduced by conversion of metallic mercury to complexed species and by deposition of HgS in reducing sediments, but even so, atmospheric transport is a major environmental distribution pathway for mercury (EPA, 1984a). Precipitation (wet/dry) is an important mechanism for removal of mercury from the atmosphere (EPA, 1984a). Photolysis is important in the breakdown of airborne mercurials and may be important in some aquatic systems.

Adsorption onto suspended and bed sediments is probably the most important process determining the fate of mercury in the aquatic environment. Sorption is strongest into organic material for the Hg(+2) species. Mercury in soils is generally complexed to organic compounds. Mercury is not readily leached from either organic-rich or mineral-rich soils (Rosenblatt et al., 1975). Uptake of mercury in plants can occur with the highest concentrations generally found in bulb or root crops (Rosenblatt et al., 1975). Turf grass exposed to a mixture of mercurous and mercuric chloride added to the root zone did not accumulate mercury (EPA, 1984a). Uptake of mercury vapor by wheat leaves has been observed (EPA, 1984a).

Virtually any mercury compound can be remobilized in aquatic systems by microbial conversion to methyl and dimethyl forms. Conditions reported to enhance biomethylation include large amounts of available mercury, large numbers of bacteria, the absence of strong complexing agents, near neutral pH, high temperatures, and moderately aerobic environments.

Inorganic mercury is bioaccumulated by numerous organisms (EPA, 1984b). In freshwater, BCFs for mercury in mercuric chloride range from 1,800 in rainbow trout (Salmo Gairdneri) to 4,994 in the fathead minnow (Pimephales promelas) (EPA, 1984b). ASTM (1985) indicates that chemicals with BCFs less than approximately 100 have low potential for causing harm to wildlife and human health via biomagnification of residues up food chains. The magnitude of the reported concentration factors suggests that appreciable bioconcentration or biomagnification of mercury can occur.

Health Effects

Occupational studies indicate that the chronic exposure to mercury vapor (Hg°) affects primarily the central nervous system and the kidneys (increased urinary excretion of high molecular weight proteins) (EPA, 1984a). Acute exposure to high vapor concentrations can cause erethism (behavioral effects), metal fume fever, pneumonitis, bronchitis, chest pains, dyspnea, coughing, stomatitis, gingivitis, salivation, and diarrhea (EPA, 1984a). In case reports, acute mercury vapor exposures have been shown to cause exudative alveolar and intestinal edema and erosion and desquamation and necrosis of the bronchiolar epithelium (EPA, 1984a). Contact dermatitis may result from exposure to liquid metallic mercury (EPA, 1984a). Soluble mercuric salts are highly toxic following ingestion as compared with the less soluble mercurous compounds.

In early studies, women chronically exposed to mercury vapor experienced increased frequencies of menstrual disturbances and spontaneous abortions (EPA, 1984a). Rats exposed to mercury vapors (2.5 mg/m^3, 6 hr/day, 5 day/week) exhibited longer estrus cycles (EPA, 1984a). Inorganic mercuric mercury (Hg^{++}) is translocated across the blood-brain and placental barriers to a lesser degree than Hg°, and therefore inorganic salts are less likely to affect the central nervous system and the fetus (EPA, 1984a). Infants 4 to 30 months appear to be more susceptible than adults and older children to the effects of mercury vapors (EPA, 1984a). Placental transport of mercury and subsequent oxidation in fetal tissues has been demonstrated in mice (EPA, 1984a). However, no conclusive results concerning the teratogenic effects of mercury vapor are available (EPA, 1984a). Parenteral administration of inorganic mercury salts has produced abnormalities in experimental animals (EPA, 1984a). A number of abnormalities were reported in hamster fetuses given a subcutaneous dose of mercury acetate on day 8 of gestation, including pericardial cavity distension, cleft palate, hydrocephalus, and heart defects (EPA, 1984a).

Mutagenic responses have been equivocal following exposure of nonmammalian cell cultures to mercuric salts in vitro (EPA, 1984a). Chromosomal aberrations have been observed in lymphocytes of persons occupationally exposed to mercury vapors (EPA, 1984a). Carcinogenesis in humans has not been associated with occupational exposure to mercury vapors (EPA, 1984a). Mercury has been classified according to EPA's Guidelines for Carcinogenic Risk Assessment in EPA's Group D (not classified) based upon inadequate data in animals and humans (50 Federal Register 46972, Wed. Nov. 13, 1985).

Toxicity to Wildlife and Domestic Animals

The aquatic toxicity of inorganic mercury compounds has been investigated. Among freshwater species, the 96-hour LC_{50} values for inorganic mercuric salts range from 0.02 ug/liter for crayfish to 2,000 ug/liter for caddis fly larvae (EPA, 1980). Mercuric chloride is acutely toxic to rainbow trout at about 300 ug/liter at 10°C (EPA, 1984a).

The acute oral lethal dose (low) in rabbits is 40 mg/kg (NIOSH, 1982). Chronic dietary exposure of chickens to mercuric chloride at growth inhibitory levels causes immune suppression with a differential reduction effect on specific immunoglobulins (Bridger and Thaxton, 1983). The LC_{50} values for mercuric chloride administered in the diets of Japanese quail (Coturnix c. japonica), ringed-neck pheasants (Phasianus colchicus), and mallard ducks (Anasplatyrhynchos) were 5,926, 3,790, and >5,000 ppm, respectively (Hill et al., 1975).

Regulations and Standards

Ambient Water Quality Criteria (EPA, 1986):

Aquatic Life (Freshwater)

Acute toxicity: 2.4 ug/liter

Chronic toxicity: 0.012 ug/liter

Aquatic Life (Saltwater)

Acute toxicity: 2.1 ug/liter

Chronic toxicity: 0.025 ug/liter

Human Health

Criterion: 144 ng/liter

National Primary Drinking Water Standard: 0.002 mg/liter (40 CFR Part 141)

NIOSH Recommended Standard: TWA inorganic mercury = 0.05 mg/m^3

OSHA Standard (skin): Ceiling Level = 0.1 mg/m^3

ACGIH TLV: TWA (vapor) = 0.05 mg/m^3
TWA (aryl and inorganic compounds) = 0.1 mg/m^3

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health nor pose a risk of cancer occurrence greater than a predetermined risk level.

For inorganic mercury the D_T value for oral exposure is based on the RfD of 3×10^{-4} mg/kg/day reported in the Health Effects Assessment Summary Table (HEAST) (EPA, 1990). Though details on the underlying study were not available, the effect of concern was central nervous system effects associated with a blood mercury level of 200 mg/ml in exposed humans (EPA, 1990). An UF of 10 was included in the derivation of the RfD, presumably to protect sensitive human subgroups.

The inhalation D_T is based on a recently verified inhalation RfD of 3.0×10^{-4} mg/m^3 (ECAO, 1990). Converting this value to a mg/kg-day dose based on a reference breathing rate of 20 m^3/day for a 70 kg human, yields an inhalation RfD of 8.6×10^{-5} mg/kg-day.

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METHYLENE CHLORIDE[1]

Summary

Methylene chloride (dichloromethane) increased the incidence of lung and liver tumors and sarcomas in exposed rats and mice. Methylene chloride yielded positive results in mutagenicity tests utilizing bacterial test systems. In humans, methylene chloride irritates the eyes, mucous membranes, and skin. Exposure to high levels adversely affects the central and peripheral nervous systems and the heart. In experimental animals, methylene chloride is reported to cause kidney and liver damage, convulsions, and paresis (incomplete paralysis).

CAS Number: 75-09-2

Chemical Formula: CH_2Cl_2

IUPAC Name: Dichloromethane

Important Synonyms and Trade Names: Methylene dichloride, methane dichloride

Chemical and Physical Properties

Molecular Weight: 84.93

Boiling Point: 40°C (EPA, 1979)

Melting Point: -95.1°C

Specific Gravity: 1.3266 at 20°C

Solubility in Water: 13,200-20,000 mg/liter at 25°C (EPA, 1979)
19,000 mg/liter (Valvani et al., 1980)

Solubility in Organics: Miscible with alcohol and ether

Log Octanol/Water Partition Coefficient (Kow): 1.25 (EPA, 1979)
1.30 (EPA, 1986a)

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[1] Compiled from: U.S. Environmental Protection Agency, Office of Waste Program Enforcement. September 1985a. Chemical, physical,and biological properties of compounds present at hazardous waste sites. A Final Report Prepared by Clement Associates, Inc.,Arlington, Virginia.

Also: USAMBRDL. 1985. Physical/Chemical and Toxicological Summaries for 62 Rocky Mountain Arsenal Contaminants. USAMBRDL. Fort Detrick, Frederick, MD.

Soil to Water Partition Coefficient (Koc):

27.5	(Sabljic, 1984) (experimental)
114; 121	(Lyman et al., 1982) Eqn 4-8 (log Kow = 1.25;1.30)
27; 30	(Lyman and Loreti, 1987) (log Kow = 1.25; 1.30)
8.8	(EPA, 1986a)

Bioconcentration Factor:

2.9 - 2.3	(Davies and Dobbs, 1984) Eqn A (S = 13,200 - 20,000)
5.25	(Lyman et al., 1982) Eqn 5-2 (log Kow = 1.25)
8.60	(Davies and Dobbs, 1984) Eqn C (log Kow = 1.25)
5.81	(Davies and Dobbs, 1984) Eqn B (log Kow = 1.25)
16.4	(Lyman et al., 1982) Eqn 5-2 (log Kow = 1.9)
21	(Davies and Dobbs, 1984) Eqn B (log Kow = 1.9)
14.2	(Davies and Dobbs, 1984) Eqn C (log Kow) = 1.9)

Vapor Pressure: 362 mm Hg at 20°C (EPA, 1986a)
436 mm Hg at 25°C (Berkowitz et al., 1978)

Vapor Density: 2.93

Henry's Law Constant: 2.6×10^{-3} atm-m^3/mole (Calculated)
2.03×10^{-3} atm-m^3/mole (EPA, 1986a)
8.53×10^{-2} Dimensionless

Transport and Fate

Volatilization to the atmosphere appears to be the major mechanism for removal of methylene chloride from aquatic systems and its primary environmental transport process (EPA, 1979). Photooxidation in the troposphere appears to be the dominant chemical fate of methylene chloride following its release to the air. Once in the troposphere, the compound is attacked by hydroxyl radicals, resulting in the formation of carbon dioxide, and to a lesser extent, carbon monoxide and phosgene. Phosgene is readily hydrolyzed to HCl and CO_2. About one percent of tropospheric methylene chloride would be expected to reach the stratosphere where it would probably undergo photodissociation resulting from interaction with high energy ultraviolet radiation. Aerial transport of methylene chloride is partly responsible for its relatively wide environmental distribution. Atmospheric methylene chloride may be returned to the earth in precipitation.

Photolysis, oxidation, and hydrolysis do not appear to be significant environmental fate processes for methylene chloride. A range of experimental and estimated Koc is reported above and indicates that some sorption of methylene chloride to soils/sediments and dissolved organic material will occur. Pavlou (1980) estimates that sorption of volatile organic compounds will range from low to moderate. The combined high water solubility and low organic partitioning of methylene chloride suggest that this compound will exhibit a high degree of environmental mobility. Although methylene chloride is potentially

biodegradable, especially by acclimatized microorganisms, biodegradation occurs at a very slow rate.

A range of BCFs for methylene chloride is also reported above. ASTM (1985) indicates that chemicals with BCFs less than approximately 100 have low potential for causing harm to wildlife and human health via biomagnification of residues up food chains. The magnitude of the concentration factors suggest that appreciable bioconcentration or biomagnification of methylene chloride residues is not likely to occur.

Health Effects

Results of a National Toxicology Program Study on methylene chloride (EPA, 1990) indicate that it produced an increased incidence of lung and liver tumors in mice and mammary tumors in female and male rats. In a chronic inhalation study, male rats exhibited an increased incidence of sarcomas in the ventral neck region (Burek et al., 1984); however, the authors suggest that the relevance and toxicological significance of this finding is uncertain in light of available toxicity data. Methylene chloride has been classified according to EPA's Guidelines for Carcinogenic Risk Assessment, in EPA's Group B2 (probable human carcinogen), based upon positive results in animal studies and inadequate evidence in humans (EPA, 1985b).

Methylene chloride is reported to be mutagenic in bacterial test systems. It has also produced positive results in the Fischer rat embryo cell transformation test. However, it has been suggested that the observed cell-transforming capability may have been due to impurities in the test material. There is no conclusive evidence that methylene chloride exposure produces teratogenic effects.

In humans, direct contact with methylene chloride produces eye, respiratory tract, and skin irritation (EPA, 1985b). Mild poisonings due to inhalation exposure produce somnolence, lassitude, numbness and tingling of the limbs, anorexia, and light headedness, followed by rapid and complete recovery. More severe poisonings generally involve correspondingly greater disturbances of the central and peripheral nervous systems. Methylene chloride also has acute toxic effects on the heart, including the induction of arrhythmia. Fatalities reportedly due to methylene chloride exposure have been attributed to cardiac injury and heart failure. Methylene chloride is metabolized to carbon monoxide in vivo, and levels of carboxyhemoglobin in the blood are elevated following acute exposures. In experimental animals, methylene chloride is reported to cause kidney and liver damage, convulsions, and distal paresis. An oral LD_{50} value of 2,136 mg/kg, and an inhalation LC_{50} value of 88,000 mg/m^3/30 minutes are reported for the rat.

Toxicity to Wildlife and Domestic Animals

Very little information concerning the toxicity of methylene chloride to domestic animals and wildlife exists (EPA, 1980). Acute values for the freshwater species Daphnia magna, the fathead minnow, and bluegill are 224,000, 193,000, and 224,000 ug/liter, respectively. Acute values for the saltwater mysid shrimp and sheepshead minnow are 256,000 and

331,000 ug/liter, respectively. No data concerning chronic toxicity are available. The 96-hour EC_{50} values for both freshwater and saltwater algae are greater than the highest test concentration, 662,000 ug/liter.

Regulations and Standards

Ambient Water Quality Criteria (EPA, 1986b):

Available data are not adequate for establishing criteria, however, EPA does report the lowest values known to be toxic in aquatic organisms:

Aquatic Life (Freshwater)

Acute toxicity: 11,000 ug/liter

Chronic toxicity: No data are available

Aquatic Life (Saltwater)

Acute toxicity: 12,000 ug/liter

Chronic toxicity: 6,400 ug/liter

Human Health

Due to the carcinogenicity of methylene chloride the ambient water criterion is set at zero. However, estimates of the carcinogenic risks associated with lifetime exposure from ingestion of contaminated water and contaminated aquatic organisms are:

Risk	Concentration
10^{-5}	1.9 ug/liter
10^{-6}	0.19 ug/liter
10^{-7}	0.019 ug/liter

CAG Potency Slope for Inhalation Exposure (EPA, 1990): 1.4×10^{-2} $(mg/kg/day)^{-1}$

CAG Potency Slope for Oral Exposure (EPA, 1990): 7.5×10^{-3} $(mg/kg/day)^{-1}$

ACGIH TLV: TWA = 174 mg/m^3

NIOSH Recommended Standards:

TWA = 100 ppm

Peak Concentration (5 min/2 hr)= 2,000 ppm

OSHA Standards: TWA = 100 ppm
Ceiling Level = 1,000 ppm
Peak Concentration (5 min/3 hr) = 2,000 ppm

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health nor pose a risk of cancer occurrence greater than a predetermined risk level.

For carcinogens such as methylene chloride, the D_T value is based on the EPA Cancer Assessment Group's cancer potency slopes. The cancer potency slopes have been estimated for oral exposure routes and for inhalation exposure for methylene chloride. The slopes are intended to be a plausible upper bound of the potency of a carcinogen in inducing cancer at low doses. Calculation of a D_T using a cancer potency slope requires selection of an acceptable cancer risk level. A range of risk levels from 10^{-4} to 10^{-7} will be considered for all carcinogens, therefore a range of D_T values is presented. Derivation of the D_T value for methylene chloride is as follows:

$$D_T = \frac{\text{Risk Level}}{\text{Potency Slope (mg/kg/day)}^{-1}}$$

$$= \frac{1 \times 10^{-4}}{1.4 \times 10^{-2} \ \text{(mg/kg/day)}^{-1}}$$

$$= 7.1 \times 10^{-3} \text{ mg/kg/day}$$

The oral D_T values for methylene chloride were similarly computed using the oral potency slope.

The range of inhalation and oral D_T values for methylene chloride is presented below:

Risk Level	Inhalation D_T (mg/kg/day	Oral D_T (mg/kg/day)
10^{-4}	7.1×10^{-3}	1.3×10^{-2}
10^{-5}	7.1×10^{-4}	1.3×10^{-3}
10^{-6}	7.1×10^{-5}	1.3×10^{-4}
10^{-7}	7.1×10^{-6}	1.3×10^{-5}

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METHYLISOBUTYL KETONE[1]

Summary

Methylisobutyl ketone (MIBK) produced kidney damage in exposed rats. In humans, exposure has produced headaches, nausea, vomiting, and eye irritation. No information is available on the carcinogenicity, mutagenicity, reproductive toxicity, or teratogenicity of MIBK.

CAS Number: 108-10-1

Chemical Formula: $(CH_3)_2CHCH_2COCH_3$

IUPAC Name: 4-Methyl-2-pentanone

Important Synonyms and Trade Names: Hexone, isobutyl methyl ketone, isopropyl acetone, and MIBK

Chemical and Physical Properties

Molecular Weight: 100.2

Boiling Point: 117°C

Melting Point: -84.7°C

Specific Gravity: 0.7978 at 20°C

Solubility in Water: 19,000 mg/liter (Marochini, 1984)

Solubility in Organics: Soluble in chloroform, alcohol, ether, acetone, benzene, and many other organic solvents

Log Octanol/Water Partition Coefficient (Kow):
1.18
1.25 (Lyman et al., 1982) Fragment Method

Soil to Water Partition Coefficients (Koc):
1.1 (Lyman and Loreti, 1987) (S=19,000)
19 (Lyman et al., 1982) Eqn 4-5 (S = 19,000)

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[1] Compiled from: U.S. Environmental Protection Agency, Office of Waste Program Enforcement. September 1985. Chemical, physical,and biological properties of compounds present at hazardous waste sites. A Final Report Prepared by Clement Associates, Inc., Arlington, Virginia.

Also: USAMBRDL. 1985. Physical/Chemical and Toxicological Summaries for 62 Rocky Mountain Arsenal Contaminants. USAMBRDL. Fort Detrick, Frederick, MD.

Bioconcentration Factor:

6.47	(Lyman et al., 1982) Eqn 5-2 (log Kow = 1.37)
2.4	(Davies and Dobbs, 1984) Eqn A (S = 19,000)
10.1	(Davies and Dobbs, 1984) Eqn B (log Kow = 1.37)
5.81	(Davies and Dobbs, 1984) Eqn C (log Kow = 1.25)
8.60	(Davies and Dobbs, 1984) Eqn B (log Kow = 1.25)
5.25	(Lyman et al., 1982) Eqn 5-2 (log Kow = 1.25)

Vapor Pressure: 16 mm Hg at 20°C (TDB Peer Review Committee, 1984)
20.3 mm Hg at 25°C (estimated; Lyman et al., 1982)

Henry's Law Constant: 1.1×10^{-4} atm-m^3/mole (calculated)
4.6×10^{-3} Dimensionless

Vapor Density: 3.45

Flash Point: 23°C

Transport and Fate

Limited information was located on the transport and fate of methylisobutyl ketone (MIBK) in the environment. MIBK is a volatile compound: therefore, loss from environmental media due to volatilization will likely be a dominant transport process. However, because it is quite soluble in water, volatilization from water bodies or wet soil will likely be limited. In the atmosphere, MIBK may be prone to attack by hydroxyl radicals (oxidation) and/or photodissociation due to interaction with strong ultraviolet radiation.

The range of estimated Kocs is reported above and indicates that little sorption of MIBK to soils/sediments and dissolved organic material will occur. Pavlou (1980) estimates that sorption of volatile organic compounds will range from low to moderate. The combined water solubility and low organic partitioning indicate that MIBK will be a mobile environmental contaminant. Biodegradation also may be an important fate process for MIBK in the environment.

A range of estimated BCFs for MIBK is also presented above. ASTM (1985) indicates that chemicals with BCF factors less than approximately 100 have low potential for causing harm to wildlife and human health via biomagnification of residues up food chains. The magnitude of the concentration factors suggests that appreciable bioconcentration or biomagnification of MIBK residues is not likely to occur.

Health Effects

No studies on the carcinogenicity, mutagenicity, reproductive toxicity, or teratogenicity of MIBK were found in the literature reviewed. MIBK caused headaches, nausea, vomiting, and eye irritation in a number of workers exposed to concentrations of 200 to

2,000 mg/m^3. Kidney damage was observed in rats exposed to 400 mg/m^3 of MIBK for 2 weeks, but the damage appeared to be reversible. Male and female rats dosed orally with MIBK daily for 13 weeks exhibited nephrotoxicity and increased liver and kidney weights at the highest dose (1,000 mg/kg) (EPA, 1986). These same effects were exhibited to a lesser extent in rats receiving 250 mg/kg. No effects were seen at 50 mg/kg. The acute oral LD_{50} for MIBK in rats is 2,080 mg/kg.

Toxicity to Wildlife and Domestic Animals

The only study reviewed on the toxicity of MIBK to wildlife reported that the tolerance limit (TL_{50}) for brine shrimp was 1,230 mg/liter. Data on the toxicity of MIBK in terrestrial animals was not located in the literature reviewed.

Regulations and Standards

OSHA Standards (air): TWA = 240 mg/m^3

ACGIH TLV: TWA = 205 mg/m^3
STEL = 307 mg/m^3

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health nor pose a risk of cancer occurrence greater than a predetermined risk level.

For MIBK, the oral D_T value is based on the current EPA RfD (EPA, 1990a). The RfD is based on a subchronic oral toxicity study in which male and female rats were administered 0, 50, 250, or 1,000 mg/kg MIBK (gavage) daily for 13 weeks (EPA, 1986). Nephrotoxicity was generally observed for both male and female high dose rats, as were increased liver and kidney weights. However, no liver lesions were observed. The same effects were noted but to a lesser degree, in the 250 mg/kg dose group. The NOEL identified from this study was 50 mg/kg/day. An UF of 1,000 is employed to address the extrapolation of results to humans (10), intraspecies variability (sensitive subgroups), (10) and the use of a subchronic rather than a chronic experimental study (10). Derivation of the D_T value for MIBK is as follows:

$$D_T = \frac{\text{NOEL (mg/kg/day)}}{\text{UF}}$$

$$= \frac{50}{1{,}000}$$

$$= 0.05 \text{ mg/kg/day}$$

The inhalation D_T value for MIBK is based on the RfD of 2 x 10^{-2} mg/kg/day identified in the EPA HEAST (EPA, 1990b). The RfD is based on a subchronic inhalation study in which rats were exposed to MIBK for six hours/day, five days/week. The toxicological endpoint of concern was liver and kidney effects (EPA, 1990a). Though additional study details were not available, an UF of 100 was included in the derivation of the RfD by EPA.

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N-NITROSODIMETHYLAMINE[1]

Summary

N-Nitrosodimethylamine (NDMA) was carcinogenic in all animal species tested, inducing benign and malignant tumors by various routes. NDMA has been determined to be mutagenic (activated preparations) in bacterial and mammalian test systems. Systemic effects of exposure to NDMA include primarily liver and kidney damage. NDMA is an eye irritant, and direct contact causes corneal damage.

CAS Number: 62-75-9

Chemical Formula: $C_6H_6N_2O$

IUPAC Name: N,N-Dimethylnitrosamine

Important Synonyms and Trade Names: dimethylnitrosamine; NDMA; DMNA

Chemical and Physical Properties

Molecular Weight: 74.1 (Merck, 1983)

Boiling Point: 152 C (Weast, 1981)

Specific Gravity: 1.005 (Merck, 1983)

Solubility in Water: 1,000 g/liter (EPA, 1985) (infinitely water soluble)

Solubility in Organics: Soluble in alcohol and ether (Merck, 1983)

Log Octanol/Water Partition Coefficient (Kow): -0.57 (Hansch and Leo, 1979)

Soil to Water Partition Coefficient (Koc): Not Applicable

Bioconcentration Factor: Not Applicable

Vapor Pressure (mm Hg): 8.1 mm Hg at 20-30°C (EPA, 1985)

Henry's Law Constant: Not Applicable

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[1] Compiled from: USAMBRDL. 1985. Physical/Chemical and Toxicological Summaries for 62 Rocky Mountain Arsenal Contaminants. USAMBRDL. Fort Detrick, Frederick, MD.

Also: U.S. Environmental Protection Agency (EPA). 1980. Ambient Water Quality Criteria for Nitrosamines. Office of Water Regulations and Standards, Criteria and Standards Division,Washington, D.C. EPA 440/5-80-064. NTIS No. PB81-117756.

Transport and Fate

The high vapor pressure of NDMA indicates that volatilization will be an important transport process. The subsequent chemical fate of NDMA in the atmosphere is unknown. However, studies of aqueous solutions of NDMA suggest that photolysis does occur. It therefore seems likely that NDMA released to the air could photolyze in the presence of water vapors present in the atmosphere.

In aqueous solutions ranging in pH from 8-11, half-lives of 7-18 hours were observed (Polo and Chow, 1976) as compared with 4 hours in distilled water, and 1 hour or less in more acidic solutions. Under alkaline conditions, breakdown products of NDMA are dimethylamine, N_2O and N_2; under more acidic conditions, HNO_2 is formed, which can then react with dimethylamine to reform NDMA. NDMA is not hydrolyzed to an appreciable extent (Polo and Chow, 1976; EPA, 1979).

Little sorption of NDMA to soils is expected to occur given its high solubility in water. The combined low organic partitioning and high water solubility indicate that NDMA will be a mobile environmental contaminant. Leaching studies by Dean-Raymond and Alexander (1976) indicated that NDMA exhibits characteristics similar to chloride ion, and therefore it is not likely to be retained on soil. Slow breakdown by sewage microorganisms has been reported (EPA, 1979).

Some uptake of NDMA in lettuce and spinach grown in hydroponic solutions containing soil, sand, or just water was reported by Dean-Raymond and Alexander (1976). Two days following the addition and equilibration of NDMA to concentrations of 10 or 100 mg/liter, samples (leaves) were analyzed for NDMA content. Lettuce grown in sand had concentrations of 1.38 mg/kg dry weight and 14.4 mg/kg dry weight at 10 and 100 mg/liter concentrations, respectively. Lettuce grown in soil at a concentration of 100 mg/liter contained 106 mg/kg dry weight tissue. Spinach grown only in water contained 0.54 mg/kg dry weight and 5.6 mg/kg dry weight at concentrations of 10 and 100 mg/liter, respectively. Under natural conditions, however, NDMA is not commonly found in plants (EPA, 1980).

Bioconcentration data for NDMA were not located in available literature. However, given the high aqueous solubility and low organic partitioning behavior, bioconcentration would not be expected to occur.

Health Effects

NDMA is very irritating to the eyes. Direct contact causes corneal damage. Systemic effects include liver and kidney damage (OHS, 1985). Symptoms of exposure include nausea, headache, vomiting, abdominal cramps, diarrhea, fever, weakness, jaundice, and liver enlargement.

NDMA and other N-nitroso compounds are acutely toxic to both animals and humans (EPA, 1980). In experimental animals, acute exposure to NDMA produced liver lesions

within 24-48 hours; death occurred typically in three to four days (EPA, 1980). Other injuries included peritoneal and plural exudates containing high proportions of blood (EPA, 1980). In humans, exposure to NDMA results in liver damage. Necropsy of at least one victim of acute NDMA exposure revealed liver cirrhosis with regenerating nodules. Another acutely exposed subject died of bronchopneumonia.

Nitrosamines have been shown to be embryotoxic and teratogenic when administered to rats late in pregnancy, unlike nitrosamides which exhibit teratogenic effects early in pregnancy (EPA, 1980). Nitrosamines are mutagenic in test systems following metabolic activation. For example, liver microsomal preparations from mouse, rat, hamster, and man are capable of activating nitrosamines. Microsomal preparations from organs other than the liver have been shown to be ineffective in activating nitrosamines to mutagens in bacterial systems (EPA, 1980). NDMA has been reported to induce forward/reverse mutation in several bacterial species, gene recombination and conversion in Saccharomyces cerevisiae, recessive lethal mutation in Drosophila melanogaster, and chromosome aberrations in mammalian cells (EPA, 1980). Positive results were achieved in recently completed chromosome aberration tests (NTP, 1986) in Chinese hamster ovary cells. Sister chromatid exchanges were also observed in this same test system (NTP, 1986). NDMA was carcinogenic in all animal species tested, inducing both benign and malignant tumors by various routes (OHS, 1985).

The acute oral LD_{50} in rats is 26 mg/kg. The acute inhalation LC_{50} values in rats and mice are 78 and 57 ppm/4 hr, respectively (OHS, 1985).

Toxicity to Wildlife and Domestic Animals

NDMA has been shown to cause hepatocellular carcinomas in rainbow trout chronically fed contaminated diets (200-800 mg/kg) (EPA, 1980). Crayfish exposed for six months to NDMA exhibited extensive degenerations in the antennal gland at 200,000 ug/liter and hyperplasia of tubular cells in the hepatopancreas at 100,000 ug/liter NDMA (EPA, 1980). The acute values for freshwater species Daphnia magna and the bluegill are 7,760 and 5,850 ug/liter, respectively.

The acute low oral lethal dose (LD_{LO}) in dogs is 20 mg/kg. The acute low inhalation concentration (LC_{LO}) in dogs is 16 ppm/4 hr (OHS, 1985). The acute oral LD_{50} in hamsters is 28 mg/kg.

Regulations and Standards

Ambient Water Quality Criteria (EPA, 1986):

> The available data are inadequate for establishing specific criteria. However, EPA does report the lowest values known to be toxic in aquatic organisms:

Aquatic Life (Freshwater):

Acute Toxicity: 5,850 ug/liter

Chronic Toxicity: No data available

Aquatic Life (Saltwater):

Acute Toxicity: 3,300 mg/liter

Chronic Toxicity: No data available

Human Health:

Due to the carcinogenicity of NDMA the ambient water criterion in set at zero. Estimates of the carcinogenic risks associated with lifetime exposure from ingestion of contaminated water and contaminated aquatic organisms are:

Risk	Concentration
10^{-4}	140 mg/liter
10^{-5}	14 mg/liter
10^{-6}	1.4 mg/liter
10^{-7}	0.14 mg/liter

CAG Potency Slope for Oral Exposure (EPA, 1990): 51 $(mg/kg/day)^{-1}$

CAG Potency Slope for Inhalation (EPA, 1990): 51 $(mg/kg/day)^{-1}$

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health nor pose a risk of cancer occurrence greater than a predetermined risk level.

For carcinogens such as NDMA, the oral and inhalation D_T values are based on the EPA Cancer Assessment Group's cancer potency slopes. The cancer potency slopes have been estimated for oral exposure routes and for inhalation exposure for some chemicals. The slopes are intended to be a plausible upper bound of the potency of a carcinogen in inducing cancer at low doses. Calculation of a D_T using a cancer potency slope requires selection of an acceptable cancer risk level. A range of risk levels from 10^{-4} to 10^{-7} is considered for all carcinogens, therefore a range of D_T values is presented. Derivation of the oral and inhalation D_T values for NDMA is as follows:

$$D_T = \frac{\text{Risk Level}}{\text{Potency Slope (mg/kg/day)}^{-1}}$$

$$= \frac{1 \times 10^{-4}}{51 \text{ (mg/kg/day)}^{-1}}$$

$$= 1.96 \times 10^{-6} \text{ mg/kg/day}$$

The range of D_T values for NDMA is presented below:

Risk Level	D_T Oral Exposure (mg/kg/day)	D_T Inhalation Exposure (mg/kg/day)
10^{-4}	2.0×10^{-6}	2.0×10^{-6}
10^{-5}	2.0×10^{-7}	2.0×10^{-7}
10^{-6}	2.0×10^{-8}	2.0×10^{-8}
10^{-7}	2.0×10^{-9}	2.0×10^{-9}

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1,4-OXATHIANE[1]

Summary

1,4-Oxathiane is a volatile and water soluble heterocyclic compound. No data on the toxicity of 1,4-Oxathiane to humans was located in available literature. Additionally, no information on the subchronic, chronic, or reproductive toxicity of 1,4-Oxathiane in animals or data on the mutagenicity or carcinogenicity were located. The acute oral LD_{50} values in male and female rats are 3,328 and 3,000 mg/kg, respectively.

CAS Number: 15980-15-1

Chemical Formula: $O(CH_2CH_2)S$

IUPAC Name: 1,4-Thioxane

Important Synonyms and Trade Names: Thioxane

Chemical and Physical Properties

Molecular Weight: 104.1 (Sax, 1979)

Boiling Point: 148.7°C (Sax, 1979)

Melting Point: -17°C (Buckingham, 1982)

Specific Gravity: 1.11 (Berkowitz et al., 1978)

Solubility in Water: 20,000 mg/l

Log Octanol/Water Partition Coefficient (Kow): -0.16 (Lyman et al., 1982) Fragment Method

Soil to Water Partition Coefficient (Koc): Not Applicable

Bioconcentration Factor: Not Applicable

Vapor Pressure (mm Hg): 5.1 mm Hg at 25°C (Merck, 1983)
3.9 mm Hg at 20°C (Berkowitz et al., 1978)

Henry's Law Constant: Not Applicable

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[1] Compiled from: USAMBRDL, 1985. Physical, Chemical, and Toxicological Data Summaries for 62 Compounds Present at Rocky Mountain Arsenal. USAMBRDL. Fort Detrick, Frederick, MD.

Transport and Fate

The vapor pressure of 1,4-Oxathiane indicates that volatilization from environmental media is likely to be a major transport pathway. However, the very high water solubility of 1,4-Oxathiane will likely offset appreciable volatilization (Berkowitz et al., 1978). No data was available on the chemical fate of 1,4-Oxathiane in water or air. Little sorption of 1,4-Oxathiane to soils is expected to occur given its high solubility in water. The combined low organic partitioning and high water solubility suggest that 1,4-Oxathiane will be a mobile environmental contaminant.

Bioconcentration data were not located for 1,4-Oxathiane in available literature. However, given the high aqueous solubility and low organic partitioning behavior, bioconcentration would not be expected to occur. Data on the persistence of 1,4-Oxathians were not located in available literature.

Health Effects

No data on the toxicity of 1,4-Oxathiane to humans were located in available literature. The LD_{50} for 1,4-Oxathiane in groups of male rats was 3,328 mg/kg (Mayhew and Muni, 1986). No acute LD_{50} could be computed for female rats. The combined LD_{50} value for both sexes was 3,123 mg/kg based on an estimated female LD_{50} of 3,000 mg/kg (Mayhew and Muni, 1986). Antemortem observations included: coma, polypnea, lacrimation, dyspnea, lethargy, ataxia, cyanosis, squinted eyes, epistaxis, wheezing, decreased body temperature, piloerection, hunched posture, and alopecia. Necropsy of animals which died revealed discolored intestines and intestinal contents of nearly all animals. Additionally, gaseous stomachs or intestines, discolored stomach contents, and distended and discolored urinary bladders were seen in some animals (Mayhew and Muni, 1986).

Exposure to undiluted 1,4-Oxathiane resulted in slight skin irritation and moderately severe eye irritation in rabbits (Berkowitz et al.,1978).

Toxicity to Wildlife and Domestic Animals

No data was located in available literature.

Regulations and Standards

None Located.

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health nor pose a risk of cancer occurrence greater than a predetermined risk level.

For 1,4-Oxathiane, the D_T value is derived from an acute oral LD_{50} value in rats (Mayhew and Muni, 1986). The D_T value is computed as the product of the acute value and an interim application factor of 1×10^{-5} (Layton et al., 1987). The application factor allows the derivation of an acceptable long-term intake rate (D_T) based on the results of acute tests in the absence of more suitable long-term studies (i.e., chronic studies). The application factor corresponds to the cumulative percentile on a lognormal distribution of $NOEL/LD_{50}$ ratios for various chemicals. The percentile was chosen to reduce the probability that the calculated dose rate would be above a toxic level; the 5th cumulative percentile was used by Layton et al. (1987) and was found to be equal to 10^{-3}. The application factor also includes a safety factor of 100 to address interspecies and intraspecies variability; therefore, an interim estimate of D_T is obtained when the application factor is multiplied by the acute value. Derivation of this D_T value is as follows:

D_T = Acute LD_{50} x Application Factor
= 3,000 mg/kg/day x 1×10^{-5}
= 0.03 mg/kg/day

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PARATHION[1]

Summary

Parathion, an organophosphorus pesticide, is acutely toxic in both animals and humans. The primary mode of toxicity following both acute and chronic exposures is via inhibition of the enzyme acetylcholinesterase in the peripheral and central nervous systems. Parathion has yielded both positive and negative results for mutagenic activity in different test systems. The result of carcinogenicity testing was negative in long-term feeding studies with mice and equivocal in studies utilizing rats.

CAS Number: 56-38-2

Chemical Formula: $CH_{10}H_{14}NO_5PS$

IUPAC Name: 0,0-diethyl 0-p-nitrophenyl phosphorothioate

Important Synonyms and Trade Names: Ethyl parathion; phosphorothioc acid 0,0-diethyl 0 (4-nitrophenyl) ester

Chemical and Physical Properties

Molecular Weight: 291

Melting Point: 6°C (Merck, 1983)

Boiling Point: 375°C (Merck, 1983)

Specific Gravity: 1.26 (Merck, 1983)

Solubility in Water: 20 mg/liter (Merck, 1983)
24 mg/liter (TDB Peer Review Committee, 1984)

Solubility in Organics: Soluble in alcohols, esters, ethers, ketones, and aromatic hydrocarbons (Merck, 1983)

Log Octanol/Water Partition Coefficient (Kow): 3.9 (Briggs, 1981)
3.8 (Rao and Davidson, 1983)

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[1] Compiled from: USAMBRDL, 1985. Physical/Chemical and Toxicological Summaries for 62 Rocky Mountain Arsenal Contaminants. USAMBRDL. Fort Detrick, Frederick, MD.

Soil to Water Partition Coefficient (Koc):

600	(Briggs, 1981) Table III (experimental)
2,961	(Lyman et al., 1982) Eqn 4-8 (log Kow = 3.85)
2,878	(Lyman and Loreti, 1987) (log Kow = 3.85)
3,651	(Kadeg et al., 1986) (log Kow = 3.85)
10,650	(Rao and Davidson, 1983) Table 1 (Mean of four soils)

Bioconcentration Factor:

497	(Lyman et al., 1982) Eqn 5-2 (log Kow = 3.82)
315	(Davies and Dobbs, 1984) Eqn B (log Kow = 3.87)
463	(Lyman et al., 1982) Eqn 5-2 (log Kow = 3.81)
571	(Lyman et al., 1982) Eqn 5-2 (log Kow = 3.93)
108	(Davies and Dobbs, 1984) Eqn 3 (S = 22)
167	(Davies and Dobbs, 1984) Eqn A (log Kow = 3.87)
132	(Davies and Dobbs, 1984) Eqn C (log Kow = 3.9)
328	(Davies and Dobbs, 1984) Eqn C (log Kow = 3.9)
542	(Lyman et al., 1982) Eqn 5-2 (log Kow = 3.9)
31-232	(EPA, 1986) Experimental Data (Brook trout muscle)
33-201	(EPA, 1986) Experimental Data (Fathead minnow whole-body)
27	(EPA, 1986) Experimental Data (Bluegill muscle)

Vapor Pressure (mm Hg): 3.78×10^{-5} mm Hg at 20°C (Merck, 1983)
0.57×10^{-5} mm Hg (EPA, 1975)
3.8×10^{-5} mm Hg (TDB Peer Review Committee, 1984)

Henry's Law Constant: 1.1×10^{-6} atm-m^3/mole (calculated)
7.9×10^{-7} atm-m^3/mole (calculated)
3.3×10^{-5} Dimensionless

Transport and Fate

The vapor pressure of Parathion suggests that minimal volatilization of this chemical from environmental media will occur. Soil temperatures and moisture content will play a large role in controlling volatilization processes (EPA, 1975).

In water, the persistence of Parathion is pH dependent. Parathion is quite stable in waters with pH 1-7 (EPA, 1975). At 10°C and pH 1-5, the half-life of Parathion was 1,000 days, while at 70°C under identical pH conditions the half-life was 1.7 days (EPA, 1975). At higher pHs (i.e., above neutral) hydrolysis of Parathion proceeds rapidly (EPA, 1975).

Numerous studies have reported Parathion persistence in soils for periods ranging from weeks to years (Menzie, 1980). Trace levels of Parathion were found 325 days following its application at 100 lb/acre to a sandy loam soil of pH 6.8 (Menzie, 1980). Two lower

application rates (2 and 12 lbs) were nondetectable after 16 and 79 days, respectively. Approximately 3.2 percent of an initial applied concentration of Parathion (15.7 ppm per year/5 years) was reportedly detectable at the end of five years (Menzie, 1969). Residues of Parathion (0.2 kg/ha) were also still detectable 16 years following its application at a rate of 176 kg/ha in another study (Menzie, 1980).

The persistence of Parathion can vary according to soil type. In general, over a range of pHs studied (6.7-8.7), persistence of Parathion was greater in those soils having higher organic carbon contents such as clays and silt loams (Menzie, 1980). Persistence (i.e., 50 days following application) ranged from 0.7 ppm Parathion in a sandy loam (initial concentration 470 ppm, 0.1 percent organic carbon) to 25 ppm in a windy loam (initial concentration 450 ppm, 10.8 percent organic carbon) (Menzie, 1980). In more alkaline soils Parathion will be degraded more rapidly, while in acidic soils, persistence will be considerably greater.

A range of estimated and experimental Koc is reported above and indicates that sorption of Parathion to soils/sediments and dissolved organic material will occur. The combined water solubility and organic partitioning data suggest that Parathion will exhibit a relatively low degree of environmental mobility.

A range of estimated and experimental BCFs for Parathion is also reported above. ASTM (1985) indicates that chemicals with BCFs less than approximately 100 have low potential for causing harm to wildlife and human health via biomagnification of residues up food chains. In light of the magnitude of the reported BCF values, it appears that magnification of Parathion residues in higher vertebrates may occur.

Health Effects

The principal mode of toxicity of Parathion in mammals is through inhibition of the enzyme acetylcholinesterase (ChE). Inhibition is increased by the oxidative conversion of Parathion to paraoxon in vivo (Casarett and Doull, 1980). Symptoms of systemic poisoning include chest tightness, wheezing expiration (due to broncho-constriction), salivation, lacrimation, sweating, increased peristalsis, nausea, vomiting, abdominal cramps, diarrhea, bradycardia, frequent and involuntary urination (due to contraction of smooth muscle in the bladder), weakness, dyspnea, and elevated blood pressure (Casarett and Doull, 1980).

Rider et al. (1969) administered Parathion to prison volunteers at dosages of 0.043, 0.064, 0.086, and 0.11 mg/kg/day (assuming 70 kg reference weight) for between 30 and 42 days. Plasma ChE was inhibited in one subject in the high dose group on day 4 and in all subjects by day 16. The lower dosages resulted in only slight decreases in plasma ChE activity.

Dogs administered concentrations of 0.021, 0.047, or 0.117 mg/kg/day Parathion in their diets for 24 weeks experienced significantly decreased levels of plasma cholinesterase at all dose levels. At the two higher dose levels, plasma cholinesterase was inhibited by 60-70

percent (NAS, 1977--Cite: Frawley and Tuyat, 1957). Rats fed Parathion for 84 days experienced slight decreases in plasma cholinesterase at levels of 0.04 and 0.06 mg/kg/day. No effect was seen at 0.02 mg/kg/day (NAS, 1977--Cite: Edson, 1964). In a study where dogs were administered 1, 2, or 3 mg/kg/day Parathion in capsules six days/week for 90 days, the medium dose group (2 mg/kg/day) lived for three weeks and exhibited unspecified signs of toxicity continuously. Animals in the two remaining dose groups survived and exhibited nervous and irritable behavior only during the early stages of treatment. No gross pathology was evident but degenerative liver changes were observed following histopathologic determinations (NAS,1977--Cite: Hazelton and Holland, 1950).

Female rats injected intraperitoneally with 3 or 3.5 mg/kg Parathion during day 11 of gestation experienced mortality, an increased number of resorptions, reduced number of fetuses per litter, and reductions in fetal and placental weights (NIOSH, 1983). Additionally, twenty-four day-old progeny of female rats administered 0.01, 0.1, or 1.0 mg/kg/day Parathion during days 2-15 of gestation experienced reductions in pseudocholinesterase and plasma renin as well as altered electrocardiograms (IARC, 1982). Rats given 10, 20, or 50 mg/kg/day Parathion over a period of two generations exhibited reduced litter sizes at birth and high postnatal mortality during the first generation at 20 and 50 mg/kg and increased pup mortality at 10 mg/kg in the second generation (IARC, 1982). Parathion was embryocidal following its administration to mice on gestational days 12, 13, and 14 (Casarett and Doull, 1980).

Chromosomal abnormalities were reported in guinea pigs injected intratesticularly with 0.05 mg Parathion (NAS, 1977--Cite: Dikshith,1973). Rats orally administered 10 mg/kg Parathion over a period of 28 days exhibited damage to DNA including strand breaks and crosslinks (NIOSH, 1983), as did mice at 20 mg/kg (oral) over the same exposure duration. Rats and mice injected intraperitoneally (3 ug/kg Parathion) also exhibited DNA strand breaks and crosslinks (NIOSH, 1983). Negative results are also reported in various mammalian and bacterial systems including E. coli pol, Salmonella (activated), S. marcescens, S. cerevisiae, Drosophila, W138 human fibroblasts, and a dominant lethal assay in mice exposed via diet or intraperitoneal injection (USAMBRDL, 1985). Studies on the carcinogenicity of Parathion in mice have not indicated any increase in tumor formation (NIOSH, 1983), though in an NCI bioassay utilizing rats the results were considered equivocal. EPA has classified Parathion according to its Guidelines For Carcinogenic Risk Assessment in Group C (possible human carcinogen).

Parathion is highly acutely toxic in both humans and animals. The lethal dose in humans is 0.24 mg/kg (NIOSH, 1983). In rats, the oral LD_{50} is 2 mg/kg and 6 mg/kg in the mouse (NIOSH, 1983). The dermal LD_{50} in mice is 32.4 mg/kg (NIOSH, 1983).

Toxicity to Wildlife and Domestic Animals

Parathion is acutely toxic to a variety of freshwater organisms. Immature amphipods (Gammarus spp.) exhibited sensitivity to Parathion at concentrations ranging from 0.25 - 0.62 ug/liter. Mature amphipods appeared to be less affected with an LC_{50} of 3.5 ug/liter (EPA, 1986). First instar cladocerans also exhibited high sensitivities to Parathion with

LC_{50} values ranging from 0.47 - 0.60 ug/liter. Adults were slightly less sensitive, with LC_{50} values ranging from 1.0 - 1.8 ug/liter. The greatest disparity in sensitivity between adults and juveniles occurred in the crayfish (Orconectes nais). An early instar was 375 times more sensitive to Parathion than were adults (EPA, 1986). The LC_{50} for the crayfish instar was 0.04 ug/liter. Acute toxicity data for 31 freshwater species indicate that the most sensitive genus, Orconectes, is over 130,000 times more sensitive than the most resistant, Tubifex and Limnodrilus, which both had LC_{50} values of 5,230 ug/liter (EPA, 1986). Fathead minnows (Pimephales promelas) were significantly affected by chronic exposure to Parathion at concentrations of 9 ug/liter.

Subchronic toxicity of Parathion in some domestic animals has been summarized by National Academy of Science (NAS, 1977). In goats, oral doses of 8 mg/kg/day were lethal following 11 days of administration. Cattle fed Parathion in capsules at doses of 0.022 and 0.112 mg/kg/day for 81 days exhibited no noticeable adverse effects. In another study with cattle, 0.11 and 0.89 mg/kg/day were also reported to produce no noticeable adverse effects.

In avian species such as the Japanese quail (Coturnix japonica), Parathion (27 ppm) inhibited egg production and resulted in reduced hatchability (Shellenberger et al., 1968). Mallard ducks (Anas platyrhyncos) fed Parathion at doses of 10 ppm experienced no adverse effects other than a reduction in mean shell thickness (NAS, 1977--Cite: Mueller and Lochman, 1972).

The acute oral LD_{50} value in dogs is 3 mg/kg and 0.93 mg/kg for cats (NIOSH, 1983). In rabbits and guinea pigs, the oral LD_{50} values are 10 mg/kg and 8 mg/kg, respectively (NIOSH, 1983). In horses, the oral LD_{50} value is 5 mg/kg (NIOSH, 1983). For avian species, the acute oral LD_{50} values in pigeons, quail, and ducks are 3 mg/kg, 6 mg/kg, and 2.34 mg/kg, respectively (NIOSH, 1983).

Regulations and Standards

Ambient Water Quality Criteria (EPA, 1986)

Aquatic Life (Freshwater)

Acute Toxicity: 0.065 ug/liter

Chronic Toxicity: 0.013 ug/liter

Aquatic Life (Saltwater)

Acute Toxicity: Insufficient Data

Chronic Toxicity: Insufficient Data

Human Health

No criteria established.

OSHA Standard: TWA = 0.1 mg/m^3

ACGIH TLV: TWA = 0.1 mg/m^3 (skin caution)

NIOSH Standard: 0.05 mg/m^3

NIOSH TWA. 0.05 mg/m^3

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day)that should not induce an adverse effect to human health nor pose a risk of cancer occurrence greater than a predetermined risk level.

For Parathion, the D_T value is based on the RfD of 6×10^{-3} mg/kg/day reported in the EPA Health Effects Assessment Summary Tables (EPA, 1990). The toxicological end points of concern were cholinesterase inhibition and cancer in exposed humans (EPA, 1990). Though additional study details were not available, an uncertainty factor of 10 was included in the derivation of the RfD, presumably to address sensitive human subgroups.

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SARIN[1]

Summary

Sarin is a highly toxic chemical formerly manufactured for use as a nerve agent. It is a potent inhibitor of the enzyme acetylcholinesterase in both human and mammalian systems. No data are available on the carcinogenicity of Sarin. Sarin did not increase the incidence of dominant lethal mutations in exposed and mated rats or result in fetotoxicity or teratogenic effects in the same species. It is rapidly broken down in the environment and therefore is not expected to be persistent.

CAS Number: 107-44-8

Chemical Formula: $C_4H_{10}FO_2P$

IUPAC Name: Methylphosphonofluoridic acid 1-methylethyl ester

Important Synonyms and Trade Names: Fluoroisopropoxy methylphosphine oxide; GB; Isopropoxymethylphosphoryl Fluoride

Chemical and Physical Properties

Molecular Weight: 140.09 (Merck, 1983)

Melting Point: -57°C (Merck, 1983)

Boiling Point: 147°C (Merck, 1983)

Solubility in Water: Infinitely Soluble (Small, 1984)

Log Octanol/Water Partition Coefficient (Kow): 0.72 (Small, 1984)

Soil to Water Partition Coefficient (Koc): Not Applicable

Bioconcentration Factor: Not Applicable

Vapor Pressure: 1.57 mm Hg at 20°C (Sax, 1979)
2.2 mm Hg at 25°C (DA, 1982)

Henry's Law Constant: Not Applicable

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[1] Compiled from: Small, M.J. 1984. Compounds Formed From the Chemical Decontamination of HD, GB, and VX and Their Environmental Fate. Technical Report 8304. USAMBRDL, Fort Detrick, Frederick, MD. NTIS No. AD-A149515.

Also: Various literature sources cited in the text and referenced in the bibliography.

Transport and Fate

The vapor pressure of Sarin (GB) indicates that volatilization from soil surfaces will occur. The chemical fate of Sarin released to the air has not been characterized; however, reactions with atmospheric water vapor would likely result in hydrolysis. The immediate Sarin hydrolysis product is isopropyl methylphosphonate, which further reacts with water to form methyl phosphonic acid. Hydrolysis of Sarin is reported to be quite rapid (Houle et al., 1972; Small, 1984). Although reaction rates will decrease with a decrease in temperature, significant hydrolytic decomposition of GB has been reported at -15°C (Shih and Ellen, 1984). The water solubility and rapid hydrolytic degradation of Sarin indicate that its persistence in environmental media will be low (Houle et al.,1972; Rosenblatt et al., 1975). The persistence of Sarin in freshwater is pH dependent and favors more acidic conditions (DA, 1982). In one study, at 25°C and a pH of 7, the persistence of Sarin was 750 hours vs. 7.5 hours at a pH of 9.0 (DA, 1982). The hydrolysis products of Sarin (identified above) are more stable; environmental persistence of these products is expected to be greater (Rosenblatt et al., 1975).

Sass et al. (1953) and USATECOM (undated) conducted studies on the stability of Sarin in soil. In the former study, the percent of applied Sarin (0.07 gram) remaining was determined in two soils under two moisture conditions: humus soil (pH 4.5) at 2.9 and 36.8 percent moisture and loam soil (pH 6.5) at 1.4 and 12.8 percent moisture. Samples analyzed at 168 hours post-treatment indicated only 5 percent of the applied Sarin remained in the low moisture loam, while no detectable quantities were found in remaining samples. The USATECOM study, utilizing an unspecified soil type containing 1 percent moisture and an initial concentration of 1 mg/g Sarin, reported remaining Sarin residues of 13 percent, 2.6 percent, and 0.02 percent, respectively, at 3, 7, and 35 days post-treatment. Houle et al. (1972) report a rapid loss of applied Sarin (100, 1,000 ug/g soil) from three soil types (clay, sandy-clay-loam, sand). At common field conditions of 25°C, 5 percent soil moisture and a windspeed of 4 mph, the predicted half-life of 100 ug Sarin/g soil was 2 hours.

Little sorption of Sarin in soils is expected to occur given its infinite solubility in water. The rapid rate of hydrolysis for Sarin combined with its infinite water solubility indicate that chemical degradation processes will likely predominate over organic partitioning and environmental mobility of the unaltered compound.

Houle et al. (1972) report that Sarin applied directly to two types of dry vegetation (cheatgrass, budsage) was lost rapidly through evaporation. Loss of Sarin from vegetation was influenced primarily by windspeed. At a windspeed of 4 mph, applied Sarin was completely lost in two days. Translocation studies in bean plants (Houle et al., 1972) indicated that a small amount of Sarin was absorbed but was lost within a period of 24 hours. Bioconcentration data for Sarin were not located in available literature. However, given its infinite aqueous solubility and low organic partitioning behavior, bioconcentration would not be expected to occur.

Health Effects

Sarin is highly toxic and a potent inhibitor of the enzyme acetylcholinesterase in mammalian systems, including humans. The resulting excessive accumulation of acetylcholine results in overstimulation of nerves leading to the respiratory tract, cardiac muscle, gastrointestinal tract, bladder, and blood vessels. Death is usually due to respiratory paralysis. Symptoms of exposure include: lacrimation, eye pain, headache, twitching eyelids, chest tightness, salivation, fatigue, weakness, anxiety, and anorexia. More severe exposures are characterized by diarrhea, frequent urination, dyspnea, ataxia, convulsions, collapse, and paralysis.

The effects of long-term (chronic) overexposure to Sarin are not well understood. Some overexposed people have reported experiencing forgetfulness, difficulty in thinking and solving problems, disturbances in vision, and persistent muscular aches and pains (DA, 1982).

Female rats were mated and exposed to Sarin vapor at concentrations of 0.0001 or 0.001 mg/m^3 (Denk, 1975). Rats were sacrificed and necropsied at 1, 2, and 3 week intervals while one group was allowed to whelp. Other female rats were given a single intraperitoneal injection (43.8 ug/kg) on the day they were mated or on days 7, 14, and 21 after mating. Rats dosed on day 21 were allowed to whelp while others were sacrificed and necropsied 19 days after mating. No evidence of fetotoxicity or an atomical abnormalities were observed in any of the fetuses examined. In the same study, no evidence of dominant lethal mutations was observed when groups of treated male rats (13.67, 27.34, 54.75, 109.51, and 219.02 ug/kg as a single intraperitoneal injection) were mated with untreated, virgin female rats.

Some compounds structurally similar to Sarin have been shown to cause birth defects in animals (DA, 1982), however, data specific for Sarin are lacking. No data are available on the carcinogenicity or mutagenicity of Sarin.

Short-term (acute) exposure to Sarin may be fatal at very low doses. The estimated lethal dose for a human is 0.01 mg/kg (Merck, 1983). Inhalation LC_{50} values for rats and mice are 3.8 mg/kg (10 minute exposure to 220 mg min/m^3) and 5.4 mg/kg (10-minute exposure to 310 mg min/m^3), respectively (DA, 1974). The acute subcutaneous LD_{50} for mice 0.271 mg/kg (Van Meter and Karczman, 1968).

Toxicity to Wildlife and Domestic Animals

Very little data are available on the toxicity of Sarin to wild or domestic animals. Inhalation LC_{50} values for guinea pigs, rabbits, cats, dogs, pigs and monkeys are 3.14 ppm (10 minutes at 180 mg min/m^3; 1.75 ppm (10 minutes at 100 mg min/m^3), 1.05 ppm (10 minutes at 60 mg min/m^3), 0.59 ppm (10 minutes at 34 mg min/m^3), and 1.29 ppm (10 minutes at 74 mg min/m^3) (DA, 1974). Sarin is slightly less toxic following dermal exposure as indicated by the LD_{50} values for rabbits, cats, dogs, and pigs, respectively:

4.4 mg/kg (depilated), 6.2 mg/kg (depilated), 10.8 mg/kg (depilated), and 115.9 mg/kg (clipped).

Regulations and Standards

The Surgeon General of the United States recommends that pregnant women not be exposed to concentrations of Sarin exceeding 0.00003 mg/m^3 averaged over a 72-hour period (DA, 1982).

Permissible Exposure Limit (DA, 1982): TWA = 0.0001 mg/m^3

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health nor pose a risk of cancer occurrence greater than a predetermined risk level.

For Sarin, the D_T value is based on a developed army standard known as a Control Limit for the General Public (CLGP). The standard was developed by McNamara and Leitnaker (1971) based on data from studies in which animals received single parenteral doses and also from specific inhalation studies of up to six months duration involving concentrations which produced overt toxic effects. The CLGP is also recommended by the Surgeon General of the United States as a limit for exposure of sensitive subgroups such as pregnant women (DA, 1982). The CLGP is intended to be protective over an indefinite period when the maximum averaging period for ambient concentrations is 72 consecutive hours.

Derivation of the D_T value from the CLGP standard is accomplished by utilizing an equation developed by Stokinger and Woodward (1958). The equation allows the computation of an Acceptable Daily Intake (ADI or D_T) from a threshold limit value. No UF (i.e., UF=1) is included in the derivation because 1) the data already address human exposures and 2) the data reflect protection of a sensitive subgroup (i.e., pregnant women). Derivation of the D_T value for Sarin utilizing the Stokinger and Woodward equation is as follows:

$$D_T = \frac{TLV \times BR \times d \times A_A}{A_o \times UF \times BW}$$

where: TLV = Concentration in air (mg/m^3)
d = Days of experimental exposure (unspecified, 7 days/7days is assumed; therefore d = 1)
A_A = Efficiency of absorption from air (100 percent assumed)
A_o = Efficiency of absorption from oral exposure (100 percent assumed)
UF = Uncertainty factor

BR = Breathing rate (m^3/day)
BW = Reference human body weight (70 kg)
D_T = Contaminant intake rate (mg/kg/day)

$$D_T = \frac{0.0000.3 \text{ mg/m}^3 \times 20 \text{ m}^3\text{/day} \times 1 \times 1}{1 \times 1 \times 70 \text{ kg}}$$

$$= 0.00000086 \text{ mg/kg/day}$$

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SULFUR MUSTARD[1]

Summary

Sulfur mustard (mustard gas) is a highly toxic compound formerly manufactured as a chemical warfare agent. It is a highly toxic vesicant (blistering agent). Sulfur mustard is toxic via all modes of exposure and has been shown to be mutagenic, teratogenic, and carcinogenic in animals.

CAS Number: 505-60-2

Chemical Formula: $(ClCH_2CH_2)_2S$

IUPAC Name: 2,2-Dichlorodiethyl sulfide

Important Synonyms and Trade Names: Mustard gas; sulfur mustard

Chemical and Physical Properties

Molecular Weight: 159.1 (Sax, 1979)

Boiling Point: 228°C (Sax, 1979)

Melting Point: 13-14°C (Merck, 1983)

Specific Gravity: 1.27 (Merck, 1983)

Solubility in Water: 800 mg/liter (EPA, 1986)
680 mg/liter (IARC, 1975)

Solubility in Organics: Soluble in most organic solvents (Merck, 1983)

Log Octanol/Water Partition Coefficient (Kow): 1.37 (Lyman et al., 1982) Fragment Method
1.37 (EPA, 1986)

Soil to Water Partition Coefficient (Koc):

34 (Lyman and Loreti, 1987) (Kow = 1.37)
132 (Lyman et al., 1982) Eqn 4-8 (Kow = 1.37)

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[1] Compiled From: USAMBRDL, 1985. Physical/Chemical and Toxicological Summaries for 62 Rocky Mountain Arsenal Contaminants. USAMBRDL. Fort Detrick, Frederick, MD.

Also: Department of the Army (DA). 1986. Draft Occupational Health Guidelines for the Evaluation and Control of Occupational Exposure to Agent Mustard. DA Pamphlet No. 40-XX. Headquarters, Department of the Army, Washington, D.C.

Bioconcentration Factor:

6.47	(Lyman et al., 1982) Eqn 5-2 (Log Kow = 1.37)
7.35	(Davies and Dobbs, 1984) Eqn C (Log Kow = 1.37)
10.1	(Davies and Dobbs, 1984) Eqn B (Low Kow = 1.37)
15	(Davies and Dobbs, 1984) Eqn A (S = 740)

Vapor Pressure: 0.09 mm Hg at 30°C (Merck, 1983)
0.17 mm Hg at 25°C (EPA, 1986)
0.1 mm Hg (Rosenblatt et al., 1975)

Vapor Density: 5.4 (Sax, 1979)

Henry's Law Constant 2×10^{-5} atm-m^3/mole (calculated)
4.45×10^{-5} atm m^3/mole (EPA, 1986)
1.87×10^{-3} Dimensionless

Transport and Fate

The vapor pressure of sulfur mustard indicates that some volatilization from environmental media will occur. Sulfur mustard will volatilize with steam (Merck, 1983); therefore, this mode of transport may be enhanced in hot and humid environments. The subsequent chemical fate of airborne sulfur mustard is unknown.

In aqueous solution, sulfur mustard hydrolyzes rapidly to thiodiglycol. The half-life of sulfur mustard in the dissolved state is estimated to be 55 minutes at 10°C and 4 minutes at 25°C (Small, 1984). In suspension, sulfur mustard undergoes a series of competing reactions which eventually result in breakdown to thiodiglycol, but initially proceed through the formation of several sulfonium salt species.

In soil or even under water, the persistence of sulfur mustard is reported to range from 3-30 years. The long residence time is thought to be due to the formation of a compound that may be insulated from reaction with water by a sulfonium-salt layer or by the formation of a polymerized mustard-type compound (Small, 1984). A range of estimated Kocs is reported above and indicates that some sorption of sulfur mustard to soils and sediments may occur. The solubility of sulfur mustard suggests that non-hydrolyzed compound could be leached to some degree; however, the rapid rate of hydrolysis for sulfur mustard will likely preclude any environmental mobility of the unaltered compound.

No data were located on the potential for uptake of sulfur mustard by plants. A range of estimated BCFs for sulfur mustard is reported above. ASTM (1985) indicates that chemicals with BCFs less than approximately 100 have low potential for causing harm to wildlife and human health via biomagnification of residues up food chains. The magnitude of the predicted concentration factors suggests that appreciable bioconcentration or biomagnification of sulfur mustard residues is not likely to occur.

Health Effects

Sulfur mustard (mustard gas) acts as a cytotoxic agent on all tissue surfaces and is therefore hazardous through all routes of exposure (DA, 1986). Repeated exposures are reported to result in hypersensitivity to its effects. Ocular exposure results in injuries ranging from mild conjunctivitis to corneal necrosis and opacification. Skin absorption results initially in capillary hyperemia and dermal edema followed by vesication (blistering) (DA, 1986). Inhalation of mustard gas produces damage primarily to the laryngeal and tracheobronchial mucosa. Severe inhalation exposures yield congestion of the pulmonary parenchyma, edema, and atelectasis (collapse of part or all of the lung) (DA, 1986). Mustard gas reacts in vivo with proteins and nucleic acids of the lung, liver, and kidney of A/J mice (IARC, 1975).

Ingestion of sulfur mustard results in necrosis and desquamation of gastrointestinal mucosa, producing diarrhea, gastrointestinal hemorrhage, nausea, and vomiting. Systemic absorption results in injury to the bone marrow, lymph nodes, and spleen, producing leukopenia and thrombocytopenia (DA, 1986). Other systemic effects include fever, central nervous system depression, cardiac irregularities, hemoconcentration, and shock. Exposure to a mustard concentration of 0.001 mg/m^3, 24 hours/day or 0.003 mg/m^3, 8 hours/day (C_t = 1.4 mg min/m^3 per day), 5 days/week for 1 year did not produce detectable damage (systemic, local, pathological, mutagenic, teratogenic, or carcinogenic) in a variety of animal species including mice, rats, guinea pigs, rabbits, and dogs (McNamara et al., 1975). Parameters monitored during the study were blood chemistry (dogs, rabbits only), bodyweights, pathology, and carcinogenicity, sensitization (eyes, skin, respiratory), reproductive indices (live to dead ratios, number of implantation sites - rats only), and albumium/globulin ratios (dogs, rabbits only).

Mustard gas has been shown to be mutagenic and carcinogenic in animals (IARC, 1975). Mustard gas has induced mutations and chromosome rearrangements in Drosophila melanogaster (IARC, 1975). It has also induced chromosome aberrations in cultured rat tumor cell lines (lymphosarcoma), and in a host-mediated assay in male BDF_1 mice, it induced both chromosome aberrations and reverse mutations to asparagine independence following single subcutaneous doses of 100 mg/kg body weight (IARC, 1975). Mustard gas is a demonstrated carcinogen causing lung tumors in mice (the only species tested) following inhalation and intravenous exposures (IARC, 1975). Injection subcutaneously produced injection site sarcomas (IARC, 1975). In humans, prolonged exposure has been associated with cancer of the tongue, paranasal sinus, larynx, bronchus, lung, and mediastinum (DA, 1986).

From military experience and accidents, the estimated lethal concentration in humans via inhalation exposure is 50 mg/m^3 for 30 minutes, and 50 mg/m^3 for 200 minutes by dermal exposure (Rosenblatt et al., 1975). The acute intravenous LD_{50} value in mice is 8.6 mg/kg (Rosenblatt et al., 1975). The subcutaneous LD_{50} in rats is 2 mg/kg.

The range of D_T values for sulfur mustard is presented below:

Risk Level	Oral D_T (mg/kg/day)	Inhalation D_T (mg/kg/day)
10^{-4}	3.4×10^{-4}	3.4×10^{-4}
10^{-5}	3.4×10^{-5}	3.4×10^{-5}
10^{-6}	3.4×10^{-6}	3.4×10^{-6}
10^{-7}	3.4×10^{-7}	3.4×10^{-7}

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SUPONA[1]

Summary

Supona is a member of the organophosphorus class of pesticides. Its primary mode of toxicity is through inhibition of the enzyme acetylcholinesterase (ChE) in mammalian systems. Effects on reproductive parameters in exposed rats have been observed. Chronic exposures have resulted in significant ChE depression in exposed animals.

CAS Number: 470-90-6

Chemical Formula: $C_{12}H_{14}PO_4Cl_3$

IUPAC Name: 2-Chloro-1-(2,4-dichlorophenyl)vinyl diethyl phosphate

Important Synonyms and Trade Names: Chlorofenvinphos; Supona

Chemical and Physical Properties

Molecular Weight: 360 (Merck, 1983)

Melting Point: -19 to -23°C (TDB Peer Review Committee, 1984)

Specific Gravity: 1.36 at 16°C (TDB Peer Review Committee, 1984)

Solubility in Water: 145 mg/liter at 23°C (Merck, 1983)
110 mg/liter at 20°C (Berg, 1982)

Solubility in Organics: Miscible with acetone, ethanol, and propylene glycol

Log Octanol/Water Partition Coefficient (Kow): 3.11 (Briggs, 1981)

Soil to Water Partition Coefficient (Koc):
1,172 (Lyman et al., 1982) Eqn 4-8 (log Kow = 3.11)
763 (Lyman and Loreti, 1987) (log Kow = 3.11)

Bioconcentration Factor:

136 (Lyman et al., 1982) Eqn 5-2 (log Kow = 3.11)
111 (Davies and Dobbs, 1984) Eqn B (log Kow = 3.11)
65 (Davies and Dobbs, 1984) Eqn C (log Kow = 3.11)
40 (Davies and Dobbs, 1984) Eqn A (S = 130)

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[1] Compiled from: USAMBRDL. 1985. Physical/Chemical and Toxicological Summaries for 62 Rocky Mountain Arsenal Contaminants. USAMBRDL. Fort Detrick, Frederick, MD.

Vapor Pressure: 7.5×10^{-6} mm Hg at 25°C (Merck, 1983)
1.7×10^{-7} mm Hg at 25°C (Edward, 1973)
4×10^{-6} mm Hg at 20°C (TDB Peer Review Committee, 1984)

Henry's Law Constant: 3.8×10^{-9} atm-m^3/mole (calculated)
7.3×10^{-10} atm-m^3/mole (calculated)
3.1×10^{-4} Dimensionless

Transport and Fate

The low vapor pressure for Supona suggests that losses through volatilization will not be a major transport process. Hydrolysis of Supona occurs, but only very slowly. At a temperature of 38°C and a pH of 1.1, the half-life estimate for Supona is >700 hours; while at a pH of 9.1, the half-life estimate is 400 hours (TDB Peer Review Committee, 1984).

In soil (type unspecified), TDB Peer Review Committee (1984) reports an expected loss of 50 percent in a "few weeks". Following application of Supona to a sandy loam soil, 20-30 percent of the chemical remained (TDB Peer Review Committee, 1984). Similar estimates are cited in Menzie (1969, 1980). In soils treated with Supona and stored for four months at 22°C, the reported degradation products were desmethyl chlorofenvinophos (Menzie, 1969). A range of estimated Kocs is reported above and indicates that sorption of Supona to soils/sediments and dissolved organic material will occur. The combined water solubility and moderate organic partitioning data for Supona suggest that this compound will exhibit some degree of environmental mobility.

Uptake of Supona in carrots (0.4 ppm) was observed 50 days following soil application of 5.6 kg/ha (Edward, 1973).

A range of estimated BCFs for Supona is also reported above. ASTM (1985) indicates that chemicals with BCFs less than approximately 100 have low potential for causing harm to wildlife and human health via biomagnification of residues up food chains. The magnitude of the concentration factors suggests that appreciable bioconcentration or biomagnification of Supona residues is not likely to occur.

Health Effects

In humans, inhibition of plasma ChE has been demonstrated following oral and dermal exposures to Supona. A volunteer given a single oral dose of 1 mg/kg Supona exhibited temporary glycosuria (Shell Chemical Company, 1967). Erythrocyte ChE was depressed 44 percent after six hours. Twenty-six days following the initial exposure, plasma ChE of the volunteer was inhibited by 41 percent. Erythrocyte ChE recovered to within 94 percent of the pre-exposure level after 54 days, while plasma ChE returned to 100 percent of initial levels during the same period.

Plasma ChE in male and female rats was significantly depressed at all levels after one week following consumption of Supona at concentrations of 0, 10, 30, 100, or 300 ppm for up to 103 weeks (Shell Chemical Company, 1967). Cholinesterase depression remained constant except in males at 10 ppm which exhibited normal levels during the second year. During the first three months of exposure, erythrocyte ChE was inhibited only in the 30 ppm dose group. Thereafter, depression was observed at all levels but recovered in males during the second year of exposure. Females in the two high dose groups exhibited a tendency for lesser weight gains. Male and female dogs were fed Supona for two years at concentrations of 0, 30, 200, or 1,000 ppm (0, 0.75, 5, or 25 mg/kg/day). Significant depression of plasma ChE activity occurred during the first nine months of exposure at all levels (Shell Chemical Company, 1967). Levels of ChE activity returned to within control levels thereafter. Depression of erythrocyte ChE occurred at 1,000 ppm consistently for 12 weeks and was sporadic thereafter (Shell Chemical Company, 1967). A subchronic oral toxicity study in beagle dogs utilizing dose levels of 0, 0.5, 1, or 3 ppm (0, 0.0125, 0.025, or 0.075 mg/kg/day) resulted in a NOEL of 3 ppm (Shell Chemical Company, 1967).

In a three-generation reproduction study, albino rats fed concentrations of Supona at 0, 30, 100, or 300 ppm (0, 0.75, 2.5, or 7.5 mg/kg/day) exhibited effects on certain reproductive parameters (Shell Chemical Company, 1967). At the two high dose levels, interference with gestation (and possibly lactation) occurred. Effects on weanling survival rates were also observed. Only nine of 20 second generation females at 30 ppm cast litters compared with 18 of 20 control females. Twenty females exposed to 30 ppm Supona in the second and third generations also experienced a reduction in the number of litters cast (6 of 20) compared with controls (14 of 20). Data on mutagenicity and carcinogenicity of Supona were not located in available literature.

Acute oral lethality values (LD_{50}) for rats and mice fed Supona ranged from 10 to 39 mg/kg (rats) and from 117 to 200 mg/kg for mice (NIOSH, 1983; TDB Peer Review Committee, 1984).

Toxicity to Wildlife and Domestic Animals

No data was located on the toxicity of Supona to aquatic organisms. The acute oral toxicities (LD_{50}) of Supona to rabbits and guinea pigs are 500 and 125 mg/kg, respectively (NIOSH, 1983). In goats and sheep the oral LD_{50} is 71.25 mg/kg while in cattle the oral LD_{50} is 20 mg/kg.

Acute toxicity data are available for avian species such as the mallard duck (Anas platyrhyncos) the bobwhite quail (Colinusvirginianus) and the ring-necked pheasant (Phasianus colchicus). The acute oral toxicity values (LD_{50}) for these species are (respectively) 85, 80-160, and 63.5 mg/kg (Hudson et al., 1984).

Regulations and Standards

None located.

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health or should not pose a risk of cancer occurrence greater than a predetermined risk level.

For Supona, the D_T value is based on a subchronic (120 day) oral feeding study in beagle dogs (Shell Chemical Company, 1967). Groups of dogs were fed dietary concentrations of 0.5, 1.0, and 3.0 ppm Supona (0.025, 0.05, and 0.15 mg/kg/day). No effects on cholinesterases were observed. Liver function tests were normal at the conclusion of the feeding period, and autopsies failed to show any gross or histological abnormalties. The NOEL was identified as 3 ppm (0.15 mg/kg/day) (Shell Chemical Company, 1967). An UF of 1,000 is included in the derivation of the D_T value to address extrapolation of the results to humans (10), intraspecies variability (sensitive subgroups) (10), and using a subchronic rather than a chronic exposure duration (10). Derivation of the D_T for Supona is as follows:

$$D_T = \frac{\text{NOEL (mg/kg/day)}}{\text{UF}}$$

$$= \frac{0.15}{1{,}000}$$

$$= 0.00015 \text{ mg/kg/day}$$

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1,1,2,2-TETRACHLOROETHANE[1]

Summary

1,1,2,2-Tetrachloroethane has been demonstrated to induce liver tumors in mice upon oral administration. It was shown to be mutagenic in several microbial short-term assays. Embryotoxic effects and increased incidence of malformations were reported after administration to pregnant mice. In various experimental animals, acute and chronic exposures have caused adverse effects on the liver, central nervous system, and kidneys. In humans, acute exposures have resulted in central nervous system depression. At extremely high doses, fatalities have been reported. Chronic effects in humans include liver toxicity, gastrointestinal disturbances, and alterations of normal central nervous system function.

CAS Number: 79-34-5

Chemical Formula: $C_2H_2Cl_4$

IUPAC Name: 1,1,2,2-Tetrachloroethane

Important Synonyms and Trade Names: sym-Tetrachloroethane, acetylene tetrachloride, dichloro-2,2-dichloroethane

Chemical and Physical Properties

Molecular Weight: 167.85 (Weast, 1981)

Boiling Point: 146.2°C (Weast, 1981)

Melting Point: -36°C (Weast, 1981)

Specific Gravity: 1.5953 at 20°C

Solubility in Water: 2,900 mg/liter at 20°C

Solubility in Organics: Soluble in alcohol, ether, acetone, benzene, petroleum ether, carbon tetrachloride, chloroform, carbon disulfide, dimethylformamide, and oils

Log Octanol/Water Partition Coefficient: 2.56

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[1] Compiled from: U.S. Environmental Protection Agency, Office of Waste Program Enforcement. September 1985. Chemical, physical, and biological properties of compounds present at hazardous waste sites. A Final Report Prepared by Clement Associates, Inc., Arlington, Virginia.

Vapor Pressure: 5 mm Hg at 20°C

Vapor Density: 5.79

Soil to Water Partition Coefficient (Koc): 118 (Mabey et al., 1982; EPA, 1986a)

Bioconcentration Factor: 42 (EPA, 1986a)

Henry's Law Constant: 3.8×10^{-4} (Mabey et al., 1982; EPA, 1986a)

Transport and Fate

Relatively little information is available pertaining specifically to the atmospheric fate of 1,1,2,2-tetrachloroethane. Based on analogy with 1,1,1-trichloroethane, stratospheric photodissociation by high energy ultraviolet light and troposheric photoxidation via reaction with hydroxyl radicals are likely to be relatively important processes in the atmosphere. However, in aquatic systems, photolysis and oxidation do not appear to be significant fate processes for 1,1,2,2-tetrachloroethane. No information related specifically to hydrolysis of 1,1,2,2-tetrachloroethane in the environment is available, but hydrolysis studies using 1,1,1-trichloroethane have indicated an experimental half-life of six months. This decomposition was attributed almost exclusively to hydrolysis (Versar, 1979). This would suggest that hydrolysis of 1,1,2,2-tetrachloroethane may also occur slowly with a half-life ranging from several months to years (Versar, 1979). Data on the volatilization of 1,1,2,2-tetrachloroethane indicates that rapid and extensive transport from surface waters to air may occur.

Based on analogy with 1,1,1-trichloroethane, sorption of 1,1,2,2-tetrachloroethane to clay sediments is probably not an important process, although the available data is not conclusive. The log octanol/water partition coefficient of 2.56 reported for this compound indicates that sorption by organic particulates and bioaccumulation may occur; however, no adequate empirical data are available. Available information concerning related compounds suggests that biotransformation and biodegradation of 1,1,2,2-tetrachloroethane occurs in the environment, but their importance to fate and transport is not known at this time.

Health Effects

1,1,2,2-Tetrachloroethane has been demonstrated to produce a significant increase in liver tumors in mice orally administered 1,1,2,2-tetrachloroethane as low as 87 mg/kg/day (females) for 87 weeks (NCI, 1978). No statistically significant increase in mortality or in the incidence of neoplasms was observed in exposed rats. Therefore, IARC concluded that only limited evidence is available for carcinogenicity in experimental animals (IARC, 1979). This compound has shown mutagenic activity in at least two bacterial strains (S. typhimurium and E. Coli). Administration of 300-400 mg/kg/day to pregnant mice reportedly produced embryotoxic effects and caused a slight increase in the incidence of offspring malformations.

1,1,2,2-Tetrachloroethane produces a variety of acute and chronic effects in laboratory animals. The target organ of toxic action is primarily the liver. However, effects on the central nervous system, kidneys, and other tissues are also reported. High acute doses may be fatal. Fatalities in humans have been reported, primarily as a result of extremely high occupational exposures by all routes of exposure (ingestion, inhalation, or skin contact). The oral LD_{50} in rats is 250 mg/kg (NIOSH, 1984).

Chronic effects include hepatotoxicity and gastrointestinal disturbances, in addition to central nervous system effects (i.e., tremors, dizziness, headache, paralysis, and polyneuritis) (EPA, 1984).

Toxicity to Wildlife and Domestic Animals

Acute values for freshwater species range from 9,320 ug/liter for an invertebrate species to approximately 20,000 ug/liter for two species of fish. An embryo-larval test conducted with the fathead minnow yielded a chronic value of 2,400 ug/liter and an acute-chronic ratio of 8.5 for this species. Among saltwater species, acute values of 9,020 ug/liter for the mysid shrimp and 12,300 ug/liter for the sheepshead minnow are reported. Exposure to 1,1,2,2-tetrachloroethane affects chlorophyll a and cell numbers of freshwater and marine algae exposed to approximately 141,000 ug/liter and 6,300 ug/liter, respectively.

Regulations and Standards

Ambient Water Quality Criteria (EPA, 1986b):

Aquatic Life

The available data are not adequate for establishing criteria.

Human Health

Estimates of the carcinogenic risks associated with lifetime exposure to various concentrations of 1,1,2,2-tetrachloroethane in water are (EPA, 1990):

Risk	Concentration
10^{-4}	17 ug/liter
10^{-5}	1.7 ug/liter
10^{-6}	0.17 ug/liter
10^{-7}	0.017 ug/liter

ACGIH TLV: TWA = 6.9 mg/m^3 (skin)

NIOSH Recommended Standard: TWA = 5 mg/m^3

OSHA Standard: TWA = 7 mg/m^3

CAG Potency Slope for Inhalation Exposures (EPA, 1990): 2.0×10^{-1} $(mg/kg/day)^{-1}$

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health nor pose a risk of cancer occurrence greater than a predetermined risk level.

For carcinogens such as 1,1,2,2-tetrachloroethane, the D_T value was derived using the EPA Cancer Assessment Group's cancer potency slopes. Cancer potency slopes have been estimated for 1,1,2,2-tetrachloroethane for both oral and inhalation exposure routes. A cancer potency slope of 2×10^{-1} $(mg/kg/day)^{-1}$ was derived for both oral and inhalation exposures based on an observed dose-response increase of liver cancers in mice treated with 1,1,2,2-tetrachloroethane at doses up to 174 mg/kg/day (NCI, 1978; EPA, 1990). Using the cancer potency slopes, the D_T value was derived as follows:

$$D_T = \frac{\text{Risk Level}}{\text{Potency Slope } (mg/kg/day)^{-1}}$$

$$= \frac{1 \times 10^{-4}}{2.0 \times 10^{-1} \ (mg/kg/day)^{-1}}$$

$$= 5.0 \times 10^{-4} \text{ mg/kg/day}$$

The range of oral and inhalation D_T values for 1,1,2,2-tetrachloroethane is presented below:

Risk Level	D_T Oral Exposure (mg/kg/day)	D_T Inhalation Exposure (mg/kg/day)
10^{-4}	5.0×10^{-4}	5.0×10^{-4}
10^{-5}	5.0×10^{-5}	5.0×10^{-5}
10^{-6}	5.0×10^{-6}	5.0×10^{-6}
10^{-7}	5.0×10^{-7}	5.0×10^{-7}

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TETRACHLOROETHYLENE[1]

Summary

Tetrachloroethylene (PCE) induced liver tumors following oral administration to mice. PCE has also been shown to be mutagenic in bacterial systems. Reproductive toxicity was observed in pregnant rats and mice following exposure to high concentrations of PCE. Animals exposed via inhalation exhibited liver, kidney, and central nervous system damage. In humans, central nervous system depression and liver toxicity are also the principal effects exhibited following PCE exposure.

CAS Number: 127-18-4

Chemical Formula: C_2Cl_4

IUPAC Name: Tetrachloroethene

Important Synonyms and Trade Names: Perchloroethylene, PCE

Chemical and Physical Properties

Molecular Weight: 165.83

Boiling Point: 121°C

Melting Point: -22.7°C

Specific Gravity: 1.63

Solubility in Water: 150 - 200 mg/liter at 20°C

Solubility in Organics: Soluble in alcohol, ether, and benzene

Log Octanol/Water Partition Coefficient (Kow): 2.60 (Hansch and Leo, 1979)
2.53 (Veith et al., 1983)

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[1] Compiled from: U.S. Environmental Protection Agency, Office of Waste Program Enforcement. September 1985. Chemical, physical, and biological properties of compounds present at hazardous waste sites. A Final Report Prepared by Clement Associates, Inc., Arlington, Virginia.

Also: USAMBRDL. 1985. Physical/Chemical and Toxicological Summaries for 62 Rocky Mountain Arsenal Contaminants. USAMBRDL. Fort Detrick, Frederick, MD.

Soil to Water Partition Coefficient (Koc):

270; 306 (Lyman and Loreti, 1987) (log Kow = 2.53; 2.60)
360 (Chiou et al., 1979) (experimental)
567; 619 (Lyman et al., 1982) Eqn 4-8 (log Kow = 2.53, 2.6)
364 (EPA, 1986a)

Bioconcentration Factor:

49 (Davies and Dobbs, 1984) (Table 2) (experimental)
38-19 (Davies and Dobbs, 1984) Eqn A (S = 140-500)
30.6 (EPA, 1980)
55.7 (Lyman et al., 1982) Eqn 5-2 (log Kow = 2.6)
49.3 (Lyman et al., 1982) Eqn 5-2 (log Kow = 2.53)
26.9 (Davies and Dobbs, 1984) Eqn C (log Kow = 2.55)
51.3 (Davies and Dobbs, 1984) Eqn B (log Kow = 2.55)
51.1 (Lyman et al., 1982) Eqn 5-2 (log Kow = 2.55)

Vapor Pressure: 14 mm Hg at 20°C
17.8 mm Hg (EPA, 1986a)

Henry's Law Constant: 1.4×10^{-2} atm-m^3/mole (calculated)
2.59×10^{-2} atm-m^3/mole (EPA, 1986a)
1.09 Dimensionless

Transport and Fate

PCE volatilizes rapidly into the atmosphere where it reacts with hydroxyl radicals to produce HCl, CO, CO_2, and carboxylic acid. This is probably the most important transport and fate process for PCE in the environment. The half-life of PCE in air is approximately 47 days (EPA, 1984). The half-life of PCE in water may range from 1-30 days (EPA, 1986a).

The range of experimental and estimated Kocs reported above indicates that sorption of PCE to soils/sediments and dissolved organic material will occur. Pavlou (1980) estimates that sorption of volatile organic compounds will range from low to moderate. The combined water solubility and organic partitioning data indicate that PCE will exhibit some degree of environmental mobility. It is uncertain if organically bound PCE can be efficiently degraded by microorganisms.

A range of experimental and estimated BCFs for PCE is also reported above. ASTM (1985) indicates that chemicals with BCFs less than approximately 100 have low potential for causing harm to wildlife and human health via biomagnification of residues up food chains. The magnitude of the concentration factors suggests that appreciable bioconcentration or biomagnification of PCE residues is not likely to occur.

Health Effects

Health effects in humans following chronic exposure to PCE include respiratory tract irritation, nausea, headache, sleeplessness, abdominal pains, constipation, liver cirrhosis, hepatitis, and nephritis (EPA, 1984). However, central nervous system depression and liver toxicity are the principal systemic effects exhibited following PCE exposure (acute, chronic). Blair et al. (1979) observed an excess of lung, cervical, and skin cancers and slight increases in leukemia and liver cancer in a study of deceased laundry and dry-cleaning workers with known exposures to PCE, carbon tetrachloride, and trichloroethylene.

PCE was not mutagenic in several Salmonella typhimurium strains either with or without metabolic activation (NTP, 1986). It was not mutgenic in mouse lymphoma cells with or without metabolic activation and did not induce sex-linked recessive lethal mutations in Drosophila melanogaster (NTP, 1986). PCE did not induce sister chromatid exchanges or chromosomal aberrations in Chinese hamster ovary cells, with or without metabolic activation.

In male and female mice, PCE was found to produce liver cancer when orally administered by gavage (NCI, 1977). The NTP recently completed a chronic (103 week) inhalation study with PCE in rats and mice (NTP, 1986). The exposure concentrations were 0, 200, or 400 ppm for rats and 0, 100, or 200 ppm for mice. Survival of male rats was affected at the high dose, and survival of male mice was affected at both doses. Survival of female mice was reduced at 200 ppm. Both concentrations of PCE were associated with leukemia in male and female rats. PCE caused renal tubular cell hyperplasia in male rats, renal tubular cell adenomas or adenocarcinomas in male rats (not statistically significant), and renal tubular cell karyomegaly in male and female rats. One low-dose male rat had a kidney lipoma and another had a nephroblastoma. In male and female mice, PCE caused increased incidences of hepatocellular neoplasms. High-dose males had increased incidences of hepatocellular adenomas, while an increased incidence of hepatocellular carcinomas occurred at both concentrations in males and females.

As was observed in rats, PCE produced renal tubular cell karyomegaly. No neoplastic changes were observed in the respiratory tracts of either species; however, an increased incidence of squamous metaplasia was observed in the nasal cavities of dosed male rats.

Delayed ossification of skull bones and sternebrae were reported in the offspring of pregnant mice exposed via inhalation to concentrations of 2,000 mg/m^3 PCE. The exposure duration was 7 hours/day and spanned days 6-15 of gestation. In another study, increased fetal resorptions were observed following exposure of pregnant rats to PCE. Renal toxicity and hepatotoxicity were exhibited by rats following chronic inhalation exposure at levels of 1,356 mg/m^3 PCE. During the first 2 weeks of a subchronic inhalation study, exposure to concentrations of 1,622 ppm (10,867 mg/m^3) of tetrachloroethylene produced signs of central nervous system depression and cholinergic stimulation in rabbits, monkeys, rats, and guinea pigs.

Toxicity to Wildlife and Domestic Animals

PCE is the most toxic of the chloroethylenes to aquatic organisms. Limited acute toxicity data are available for PCE; however, these data appear to indicate that the LC_{50} values for saltwater and freshwater species are similar--approximately 10,000 ug/liter. The trout was the most sensitive species evaluated (LC_{50} = 4,800 ug/liter). Chronic values were 840 and 450 ug/liter for freshwater and saltwater species, respectively. An acute-chronic ratio of 19 has been computed for PCE.

No information on the toxicity of PCE to terrestrial wildlife or domestic animals was available in the literature reviewed.

Regulations and Standards

Ambient Water Quality Criteria (EPA, 1986c):

The available data are not adequate for establishing criteria. However, EPA does report the lowest values known to be toxic to aquatic organisms.

Aquatic Life (Freshwater)

Acute toxicity: 5,280 ug/liter
Chronic toxicity: 840 ug/liter

Aquatic Life (Saltwater)

Acute toxicity: 10,200 ug/liter
Chronic toxicity: 450 ug/liter

Human Health

Due to the carcinogenicity of PCE the ambient water criterion is set at zero. However, estimates of the carcinogenic risks associated with lifetime exposure from ingestion of contaminated water and contaminated aquatic organisms are:

Risk	Concentration
10^{-4}	80 ug/liter
10^{-5}	8.0 ug/liter
10^{-6}	0.8 ug/liter
10^{-7}	0.08 ug/liter

CAG Potency Slope for oral exposure (EPA, 1990): 5.1×10^{-2} $(mg/kg/day)^{-1}$

CAG Potency Slope for inhalation exposure (EPA, 1990): 3.3×10^{-3} $(mg/kg/day)^{-1}$

NIOSH Recommended Standards (air): TWA = 100 ppm
Ceiling Level = 200 ppm

ACGIH TLV: TWA = 50 ppm
STEL = 200 ppm

OSHA Standards: TWA = 170 mg/m^3

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health nor should not pose a risk of cancer occurrence greater than a predetermined risk level.

For carcinogens such as PCE the D_T value is based on the EPA Cancer Assessment Group's cancer potency slopes. The cancer potency slopes have been estimated for oral exposure routes and for inhalation exposure for PCE. The slopes are intended to be a plausible upper bound of the potency of a carcinogen in inducing cancer at low doses. Calculation of a D_T using a cancer potency slope requires selection of an acceptable cancer risk level. Arange of risk levels from 10^{-4} to 10^{-7} is considered for all carcinogens, therefore a range of D_T values is presented. Derivation of the oral D_T values for PCE is as follows:

$$D_T = \frac{\text{Risk Level}}{\text{Potency Slope (mg/kg/day)}^{-1}}$$

$$= \frac{1 \times 10^{-4}}{5.1 \times 10^{-2} \text{ (mg/kg/day)}^{-1}}$$

$$= 2.0 \times 10^{-3} \text{ mg/kg/day}$$

The inhalation D_T values for PCE were similarly computed using the inhalation potency slopes.

The range of D_T values for tetrachloroethylene is presented below:

Risk Level	D_T Oral Expose (mg/kg/day)	D_T Inhalation Exposure (mg/kg/day)
10^{-4}	2.0×10^{-3}	3.0×10^{-2}
10^{-5}	2.0×10^{-4}	3.0×10^{-3}
10^{-6}	2.0×10^{-5}	3.0×10^{-4}
10^{-7}	2.0×10^{-6}	3.0×10^{-5}

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THIODIGLYCOL[1]

Summary

Thiodiglycol is a highly water soluble and environmentally mobile sulfur compound. No subchronic or chronic toxicity data are currently available for thiodiglycol. Additionally, no data are available on reproductive toxicity, mutagenicity, or carcinogenicity. Limited acute data are available. The oral LD_{50} in guinea pigs is 3,960 mg/kg, indicating a low acute toxicity in this species.

CAS Number: 111-48-8

Chemical Formula: $C_4H_{10}O_2S$

IUPAC Name: 2,2-Thiodiethanol

Important Synonyms and Trade Names: Thiodiethylene glycol; 2,2-Thiodiethanol

Chemical and Physical Properties

Molecular Weight: 122.2 (Merck, 1983)

Boiling Point: 282°C (Sax, 1979)

Melting Point: -16°C (Merck, 1983)

Solubility in Water: Completely Soluble (Union Carbide Corp, 1970)

Log Octanol/Water Partition Coefficient (Kow): -0.77 (Small, 1984)

Soil to Water Partition Coefficient (Koc): Not Applicable

Bioconcentration Factor: Not Applicable

Vapor Pressure: 1.9×10^{-5} mm Hg at 25°C (Small, 1984)

Vapor Density: 4.21 (Sax, 1979)

Henry's Law Constant: Not Applicable

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[1] Compiled from: USAMBRDL, 1985. Physical/Chemical and Toxicological Summaries for 62 Rocky Mountain Arsenal Contaminants. USAMBRDL. Fort Detrick, Frederick, MD.

Transport and Fate

The infinite solubility of thiodiglycol in water suggests that it would be readily leached from soil. The vapor pressure of thiodiglycol indicates that volatilization is not likely to be a major transport process from environmental media. Data on the stability of thiodiglycol in air, soil, and water was not located in available literature.

Little sorption of thiodiglycol to soils or sediments is expected to occur given its high solubility in water. Therefore, thiodiglycol is likely to be an environmentally mobile contaminant.

Bioconcentration data for thiodiglycol were not located in available literature. However, given its completely soluble nature and low organic partitioning behavior, bioconcentration would not be expected to occur. No data on the uptake of thiodiglycol by plants or its subsequent bioavailability were located in the available literature.

Health Effects

No data were located on the subchronic or chronic toxicity, reproductive toxicity, teratogenicity, mutagenicity, or carcinogenicity of thiodiglycol in the available literature. Thiodiglycol is classified as a skin and eye irritant (NIOSH, 1986). Acute lethality data (LD_{50}) are available for rats, mice, rabbits, and guinea pigs (NIOSH, 1986). In rats and mice the subcutaneous LD_{50} values are 4,000 mg/kg for both animals (NIOSH, 1986). The intravenous LD_{50} in rabbits is 3,000 mg/kg. In guinea pigs the oral LD_{50} is 3,960 mg/kg.

Toxicity to Wildlife and Domestic Animals

The only available toxicity data for thiodiglycol is summarized above.

Regulations and Standards

None located.

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health nor pose a risk of cancer occurrence greater than a predetermined risk level.

For thiodiglycol, the D_T value is derived from an acute oral LD_{50} value in guinea pigs (NIOSH, 1986). The D_T value is computed as the product of the acute value and an application factor of 1×10^{-5} (Layton et al., 1987). The application factor allows the derivation of an interim acceptable long-term intake rate (D_T) based on the results of acute tests in the absence of more suitable long-term studies (i.e., chronic studies). The application factor corresponds to the cumulative percentile on a lognormal distribution of $NOEL/LD_{50}$ ratios for various chemicals. The percentile was chosen to reduce the

probability that the calculated dose rate would be above a toxic level; the 5th cumulative percentile was used by Layton et al. (1987) and was found to be equal to 10^{-3}. The application factor also includes a safety factor of 100 to address interspecies and intraspecies variability; therefore, an interim estimate of D_T is obtained when the application factor is multiplied by the acute value. Derivation of this D_T value is as follows:

D_T = Acute LD_{50} x Application Factor
= 3,960 mg/kg/day x 1 x 10^{-5}
= 0.04 mg/kg/day

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TOLUENE[1]

Summary

Toluene has been shown to be embryotoxic in experimental animals. An increased incidence of cleft palate was observed in the offspring of exposed mice. Chronic inhalation exposure to high levels of toluene caused cerebellar degeneration and an irreversible encephalopathy in animals. In humans, acute exposure yields central nervous system depression and narcosis.

CAS Number: 108-88-3

Chemical Formula: $C_6H_5CH_3$

IUPAC Name: Methylbenzene

Important Synonyms and Trade Names: Toiuol, phenylmethane

Chemical and Physical Properties

Molecular Weight: 92.13

Boiling Point: 110°C

Melting Point: -95°C

Specific Gravity: 0.8669 at 20°C

Solubility in Water: 534.8 mg/liter (EPA, 1986a)
515 mg/liter (Wilson et al., 1981)

Solubility in Organics: Soluble in acetone, ligroin, and carbon disulfide; miscible with alcohol, ether, benzene, chloroform, glacial acetic acid, and other organic solvents

Log Octanol/Water Partition Coefficient (Kow): 2.69 (Geyer et al., 1984; Moriguchi, 1975)
2.65 (Tewari et al., 1982)
2.58 (Valvani et al., 1980)
2.73 (EPA, 1986a)

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[1] Compiled from: U.S. Environmental Protection Agency, Office of Waste Program Enforcement. September 1985. Chemical, physical, and biological properties of compounds present at hazardous waste sites. A Final Report Prepared by Clement Associates, Inc., Arlington, Virginia.

Also: USAMBRDL. 1985. Physical/Chemical, and Toxicological Summaries for 62 Rocky Mountain Arsenal Conaminants. USAMBRDL. Fort Detrick, Frederick, MD.

Soil to Water Partition Coefficient (Koc):

603; 728 (Lyman et al., 1982) Eqn 4-8 (log Kow = 2.58; 2.73)
295; 386 (Lyman and Loreti, 1987) (log Kow = 2.58; 2.73)
300 (EPA, 1986a)

Bioconcentration Factor:

59 (Davies and Dobbs, 1984) Eqn B (log Kow = 2.65)
53.8 (Lyman et al., 1982) Eqn 5-2 (log Kow = 2.58)
60.8 (Lyman et al., 1982) Eqn 5-2 (log Kow = 2.65)
65.2 (Lyman et al., 1982) Eqn 5-2 (log Kow = 2.69)
18.1 (Davies and Dobbs, 1984) Eqn A (S = 525)
34 (Davies and Dobbs, 1984) Eqn C (log Kow = 2.6)
29.9 (Davies and Dobbs, 1984) Eqn C (log Kow = 2.64)
58.1 (Davies and Dobbs, 1984) Eqn B (log Kow = 2.64)
59.8 (Lyman et al., 1982) Eqn 5-2 (log Kow = 2.64)

Vapor Pressure: 28.7 mm Hg at 25°C (EPA, 1986a)

Vapor Density: 3.14

Flash Point: 4.4°C

Henry's Law Constant: 6.6×10^{-3} atm-m^3/mole (calculated)
6.37×10^{-3} atm-m^3/mole (EPA, 1986a)
2.68×10^{-1} Dimensionless

Transport and Fate

Volatilization appears to be the major route of removal of toluene from aquatic environments and atmospheric reactions of toluene probably subordinate all other fate processes (EPA, 1979). Photooxidation is the primary atmospheric fate process for toluene, and benzaldehyde is the principal organic degradation product. Subsequent precipitation or dry deposition can deposit toluene and its oxidation products into aquatic and terrestrial systems. Direct photolytic cleavage of toluene is energetically improbable in the troposphere, and oxidation and hydrolysis are probably not important as aquatic fates.

A range of estimated Kocs is reported above and indicates that sorption of toluene to soils/sediments and dissolved organic material will occur. Pavlou (1980) estimates that sorption of volatile organic compounds will range from low to moderate. The combined water solubility and organic partitioning data suggest that toluene will exhibit some degree of environmental mobility. Although toluene is known to be degraded by microorganisms and can be detoxified and excreted by mammals, the available data do not allow estimation of the relative importance of biodegradation/biotransformation processes. However,

Overcash et al., (1982) report that fungi and soil microorganisms are capable of using toluene as a carbon source. They also reported that less than 6.25 percent of applied toluene was retained in soil 1 week following application as part of a laboratory test.

A range of estimated BCFs for toluene is also presented above. ASTM (1985) indicates that chemicals with BCFs less than approximately 100 have low potential for causing harm to wildlife and human health via biomagnification of residues up food chains. The magnitude of the concentration factors suggests that appreciable bioconcentration or biomagnification of toluene residues is not likely to occur.

Health Effects

There is no conclusive evidence that toluene is carcinogenic or mutagenic in animals or humans (EPA, 1980). A long-term inhalation study in rats (CIIT, Unpublished, 1980; 50 Federal Register 47005, Wed., Nov. 13, 1985) concluded that toluene was not carcinogenic following inhalation by rats. The National Toxicological Program is currently conducting inhalation and gavage carcinogenicity bioassays in both rats and mice. Toluene has been classified according to EPA's Guidelines for Carcinogenic Risk Assessment in EPA's Group D (not classified), based on negative results in an inhalation study and inadequate data on ingestion exposure (50 Federal Register 47005).

Oral administration of toluene at doses as low as 260 mg/kg produced a significant increase in embryonic lethality in mice (EPA, 1980). Decreased fetal weight was observed at doses as low as 434 mg/kg, and an increased incidence of cleft palate was seen at doses as low as 867 mg/kg. Other researchers, however, have reported that toluene is embryotoxic but not teratogenic in laboratory animals.

Acute exposure to toluene at concentrations of 375-1,500 mg/m^3 produces central nervous system depression and narcosis in humans (ACGIH, 1980). However, even exposure to quantities sufficient to produce unconsciousness fail to produce residual organ damage. The rat oral LD_{50} value is between 5,000 and 7,000 mg/kg. The inhalation LC_{50} value in the rat varies between 33,000 and 46,000 mg/m-^{3} at 4 and 6.5 hours exposure, respectively. Chronic inhalation exposure to toluene at relatively high concentrations produces cerebellar degeneration and an irreversible encephalopathy in mammals. Toluene in sufficient amounts appears to have the potential to alter significantly the metabolism and resulting bioactivity of certain chemicals. For example, coadministration of toluene with benzene or styrene has been shown to suppress the metabolism of benzene or styrene in rats.

Toxicity to Wildlife and Domestic Animals

Of five freshwater species tested with toluene, the Cladoceran Daphnia magna was most resistant to acute effects (EPA, 1980). The EC_{50} and LC_{50} values for all five species range from 12,700 to 313,000 ug/liter. No chronic tests are available for freshwater species. The two freshwater algal species tested are relatively insensitive to toluene with EC_{50} values of 245,000 ug/liter or greater being reported. For saltwater species, EC_{50} and LC_{50} values range from 3,700 ug/liter for the bay shrimp to 1,050 mg/liter for the Pacific oyster.

The chronic value in an embryo-larval test for the sheepshead minnow is reported to be between 3,200 and 7,700 ug/liter, and the acute-chronic ratio is between 55 and 97. In several saltwater algal species and kelp, effects occur at toluene concentrations ranging from 8,000 to greater than 433,000 ug/liter.

Regulations and Standards

Ambient Water Quality Criteria (EPA, 1986b):

The available data are not adequate for establishing criteria. However, EPA does report the lowest concentrations of toluene known to be toxic to aquatic organisms.

Aquatic Life (Freshwater)

Acute toxicity: 17,500 ug/liter
Chronic toxicity: No available data

Aquatic Life (Saltwater)

Acute toxicity: 6,300 ug/liter
Chronic toxicity: 5,000 ug/liter

Human Health

Criterion: 14.3 mg/liter

National Primary Drinking Water Standard (EPA): 2.0 mg/liter (Proposed RMCL; 50 Federal Register 47005, Wed., Nov. 13, 1985).

ACGIH TLV: TWA = 377 mg/m^3
STEL = 565 mg/m^3

OSHA Standards: TWA = 375 mg/m^3
STEL = 565 mg/m^3

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health nor pose a risk of cancer occurrence greater than a predetermined risk level.

The oral D_T value for toluene is based on the current RfD (EPA, 1990). The RfD is based on a chronic (24 month) inhalation study utilizing male and female rats exposed to toluene (113, 377, or 1,130 mg/m^3) 6 hours/day, 5 days/week (CIIT, 1980). Clinical chemistry, hematology and urinalysis testing were conducted at 18 and 24 months. All parameters

were normal at termination of the study except for a dose-related reduction in hematocrit values in females exposed to 377 or 1,130 mg/m³. The identified NOAEL from this study was 1,130 mg/m³ (29 mg/kg/day). An UF of 100 is employed to address the extrapolation of results to humans (10) and to account for intraspecies variability (sensitive subgroups) (10). Derivation of theoral D_T (RfD) is as follows:

$$D_T = \frac{\text{NOAEL (mg/kg/day)}}{\text{UF}}$$

$$= \frac{29}{100}$$

$$= 0.3 \text{ mg/kg/day}$$

The inhalation D_T for toluene is also based on an EPA RfD (EPA, 1990) in which humans were exposed to 40 ppm (151 mg/m³) toluene for a period of six hours. The toxicological effects of concern involved central nervous system effects and irritation of the eyes and nose (EPA, 1990). An UF of 100 was incorporated in the derivation of the RfD to address sensitive subgroups (10) and the use of a LOEL (10). The reference concentration derived from this study was 2.0 mg/m³ (i.e., 151 mg/m³ divided by an UF of 100 and rounded). Conversion to a mg/kg-day inhalation RfD was achieved assuming a 20 m³ reference breathing rate for a 70 kg adult. The resulting inhalation reference dose for toluene is 5.7×10^{-1} mg/kg-day.

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1,1,1-TRICHLOROETHANE[1]

Summary

Preliminary results suggest that 1,1,1-trichloroethane (1,1,1-TCA) induces liver tumors in female mice. It was shown to be mutagenic using the Ames assay (Salmonella) and in cultured rat embryo cells. Inhalation exposure to high concentrations of 1,1,1-TCA depresses the central nervous system, affects cardiovascular function, and damages the lungs, liver, and kidneys in animals and humans. Irritation of the skin and mucous membranes has also been associated with human exposure to 1,1,1-TCA.

CAS Number: 71-55-6

Chemical Formula: CH_3CCl_3

IUPAC Name: 1,1,1-Trichloroethane

Important Synonyms and Trade Names: methyl chloroform, chloro-1,1,1-TCA

Chemical and Physical Properties

Molecular Weight: 133.4

Boiling Point: 74.1°C

Melting Point: -30.4°C (liquid)

Solubility in Water: 4,400 mg/liter at 20°C (Verschueren, 1977)
1,360 mg/liter (Chiou et al., 1979)

Solubility in Organics: Soluble in acetone, benzene, carbon tetrachloride, methanol, ether, alcohol, and chlorinated solvents

Log Octanol/Water Partition Coefficient (Kow): 2.47 (Davis and Dobbs, 1984)
2.5 (EPA, 1986a)

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[1] Compiled from: U.S. Environmental Protection Agency, Office of Waste Program Enforcement. September 1985. Chemical, physical, and biological properties of compounds present at hazardous waste sites. A Final Report Prepared by Clement Associates, Inc., Arlington, Virginia.

Also: USAMBRDL. 1985. Physical/Chemical and Toxicological Summaries for 62 Rocky Mountain Arsnal Contaminants. USAMBRDL. Fort Detrick, Frederick, MD.

Soil to Water Partition Coefficient (Koc):

104	(Chiou et al., 1979) Fig. 2 (experimental)
546	(Lyman et al., 1982) Eqn 4-8 (log Kow - 2.5)
256	(Lyman and Loreti, 1987) (log Kow = 2.5)
152	(EPA, 1986a)

Bioconcentration Factor:

95	(Davies and Dobbs, 1984) Eqn B (log Kow = 3.0
8	(Davies and Dobbs, 1984) (Table 2) (experimental)
31.8	(Lyman et al., 1982) Eqn 5-2 (log Kow = 2.28)
32.4	(Lyman et al., 1982) Eqn 5-2 (log Kow = 2.29)
40.7	(Lyman et al., 1982) Eqn 5-2 (log Kow = 2.42)
190	(Lyman et al., 1982) Eqn 5-2 (log Kow = 3.3)
19-10.6	(Davies and Dobbs, 1984) Eqn A (S = 480-1,360)
23-82	(Davies and Dobbs, 1984) Eqn B (log Kow = 2.3-3.3)
46	(Davies and Dobbs, 1984) Eqn B (log Kow = 3.0)
110	(Lyman et al., 1982) Eqn 5-2 (log Kow = 3.0)

Vapor Pressure: 123 mm Hg at 20°C (EPA, 1986a)
127 mm Hg at 25°C (TDB Peer Review Committee, 1984)

Vapor Density: 4.63

Henry's Law Constant: 0.044 atm-m^3/mole (calculated)
0.0144 atm-m^3/mole (EPA, 1986a)

Transport and Fate

1,1,1-TCA disperses from surface water primarily by volatilization. Following volatilization, photooxidation by reaction with hydroxyl radicals in the atmosphere is the principal fate process. Several studies have indicated that 1,1,1-TCA may be adsorbed onto organic materials in the sediment. A range of experimental and estimated Kocs is reported above and indicates that some sorption of 1,1,1-TCA to soils/sediments and dissolved organic material will occur. Pavlou (1980) estimates that sorption of volatile organic compounds will range from low to moderate. The combined water solubility and organic partitioning data for 1,1,1-TCA suggest that this compound will exhibit some degree of environmental mobility.

A range of experimental and estimated BCFs for 1,1,1-TCA is also reported above. ASTM (1985) indicates that chemicals with BCFs less than approximately 100 have low potential for causing harm to wildlife and human health via biomagnification of residues up food chains. The magnitude of the concentration factors suggest that appreciable bioconcentration or biomagnification of 1,1,1-TCA residues is not likely to occur.

Health Effects

1,1,1-TCA has been retested for carcinogencity due to early lethality in a previous study by the National Cancer Institute (NCI, 1977). Preliminary results indicate that 1,1,1-TCA increased the incidence of combined hepatocellular carcinomas and adenomas in female mice when administered by gavage (NTP, 1984). There is evidence that 1,1,1-TCA is mutagenic in Salmonella typhimurium and causes transformation in cultured rat embryo cells (EPA, 1980). These data suggest that the chemical may be carcinogenic.

Other toxic effects of 1,1,1-TCA are seen only at concentrations well above those likely in an open environment. The most notable toxic effects of 1,1,1-TCA in humans and animals are central nervous system depression, including anesthesia at very high concentrations and impairment of coordination, equilibrium, and judgment at lower concentrations (350 ppm and above); cardiovascular effects, including premature ventricular contractions, decreased blood pressure, and sensitization to epinephrine-induced arrhythmia, and adverse effects on the lungs, liver, and kidneys. Irritation of the skin and mucous membranes resulting from exposure to 1,1,1-TCA has also been reported. The oral LD_{50} value of 1,1,1-TCA in rats is approximately 11,000 mg/kg.

Toxicity to Wildlife and Domestic Animals

The acute toxicity of 1,1,1-TCA to aquatic species is rather low, with the LC_{50} concentration for the most sensitive species tested being 52.8 mg/l. No chronic toxicity studies have been conducted on 1,1,1-TCA but acute-chronic ratios for the other chlorinated ethanes ranged from 2.8 to 8.7.

The acute oral LD_{50} values for 1,1,1-TCA in rabbits and dogs are 5,660 and 750 mg/kg, respectively (Sax, 1979).

Regulations and Standards

Ambient Water Quality Criteria (EPA, 1986b):

The available data are not adequate for establishing criteria. However, EPA does report the lowest values of the two trichloroethanes (1,1,1 and 1,1,2) known to be toxic in aquatic organisms.

Aquatic Life (Freshwater)

Acute toxicity: 18 mg/liter
Chronic toxicity: No available data

Aquatic Life (Saltwater)

Acute toxicity: 31.2 mg/liter
Chronic toxicity: No available data

Human Health

Criterion: 18.4 mg/liter

National Primary Drinking Water Standard: 0.20 mg/liter (40 CFR Part 141).

NIOSH Recommended Standard: Ceiling Level = 350 ppm

OSHA Standard: TWA = 1900 mg/m^3
STEL = 2450 mg/m^3

ACGIH TLV: TWA = 1910 mg/m^3
STEL = 2460 mg/m^3

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health nor pose a risk of cancer occurrence greater than a predetermined risk level.

For 1,1,1-TCA the oral D_T is based on the current RfD of 9×10^{-2} mg/kg/day (EPA, 1990a). The RfD is derived from a 6-month inhalation study in guinea pigs which indicated no adverse effects on growth (i.e. a NOAEL) at a dose of 90 mg/kg/day (EPA, 1990a). An UF of 1,000 is employed to address the extrapolation of results to humans (10), intraspecies variability (10), and to account for the use of a subchronic rather than a chronic experimental exposure period (10). Derivation of the oral D_T value for 1,1,1-TCA is as follows:

$$D_T = \frac{\text{NOAEL (mg/kg/day)}}{\text{UF}}$$

$$= \frac{90}{1{,}000}$$

$$= 0.09 \text{ mg/kg/day}$$

The inhalation D_T for 1,1,1-TCA is based on the RfD of 3×10^{-1} mg/kg/day reported in the EPA HEAST (EPA, 1990b). The RfD is based on a subchronic inhalation study in which guinea pigs were exposed to 1,1,1-TCA 7 hours/day, 5 days/week for six months. The toxicological effect of concern was liver toxicity (EPA, 1990b). Though additional study details were not available, an UF of 1,000 was incorporated by EPA in the derivation of the RfD.

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1,1,2-TRICHLOROETHANE[1]

Summary

1,1,2-Trichloroethane (1,1,2-TCA) induced liver tumors and pheochromocytomas of the adrenal gland in mice. Liver and kidney damage occurred in dogs subacutely exposed (i.p.) to 1,1,2-TCA. It was not mutagenic when tested with the Ames (Salmonella) assay.

CAS Number: 79-00-5

Chemical Formula: $CH_2ClCHCl_2$

IUPAC Name: 1,1,2-Trichloroethane

Important Synonyms and Trade Names: Vinyl trichloride, ethane trichloride

Chemical and Physical Properties

Molecular Weight: 133.41

Boiling Point: 133.8°C
114°C (TDB Peer Review Committee, 1984)

Melting Point: -36.5°C

Specific Gravity: 1.4397 at 20°C

Solubility in Water: 4,500 mg/liter at 20°C (EPA, 1986a)

Solubility in Organics: Soluble in alcohol, ether, and chloroform

Log Octanol/Water Partition Coefficient (Kow): 2.47 (EPA, 1986a)

Soil to Water Partition Coefficient (Koc):

526 (Lyman et al., 1982) Eqn 4-8 (log Kow = 2.47)
242 (Lyman and Loreti, 1987) (log Kow = 2.47)
56 (EPA, 1986a)

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[1] Compiled from: U.S. Environmental Protection Agency, Office of Waste Program Enforcement. September 1985. Chemical, physical, and biological properties of compounds present at hazardous waste sites. A Final Report Prepared by Clement Associates, Inc., Arlington, Virginia.

Also: USAMBRDL. 1985. Physical/Chemical and Toxicological Summaries for 62 Rocky Mountain Arsenal Contaminants. USAMBRDL. Fort Detrick, Frederick, MD.

Bioconcentration Factor:

22.0	(Lyman et al., 1982) Eqn 5-2 (log Kow = 2.07)
5.4	(Davies and Dobbs, 1984) Eqn A (S = 4,400)
16	(Davies and Dobbs, 1984) Eqn C (log Kow = 2)
24	(Davies and Dobbs, 1984) Eqn B (log Kow = 2)
15.3	(Davies and Dobbs, 1984) Eqn C (log Kow = 2.07)
26.5	(Davies and Dobbs, 1984) Eqn B (log Kow = 2.07)

Vapor Pressure: 19 mm Hg at 20°C
20 mm Hg at 21.6°C (Perry and Chilton, 1973)
23.5 mm Hg at 25°C (Estimated; Lyman et al., 1982)
30 mm Hg (EPA, 1986a)

Vapor Density: 4.63

Henry's Law Constant: 9×10^{-4} atm-m^3/mole (calculated)
1.17×10^{-3} atm-m^3/mole (EPA, 1986a)
4.92×10^{-2} Dimensionless

Transport and Fate

Volatilization and subsequent photooxidation in the troposphere are probably the primary transport and fate processes for 1,1,2-TCA in aqueous media. A range of estimated Kocs is reported above and indicates that some sorption of 1,1,2-trichloroethane to soils/sediments and dissolved organic material will occur. Pavlou (1980) estimates that sorption of volatile organic compounds will range from low to moderate. The combined high water solubility and low organic partitioning suggests that 1,1,2-TCA will exhibit a high degree of environmental mobility.

A range of estimated BCFs for 1,1,2-TCA is also reported above. ASTM (1985) indicates that chemicals with BCFs less than approximately 100 have low potential for causing harm to wildlife and human health via biomagnification of residues up food chains. The magnitude of the concentration factors suggest that appreciable bioconcentration or biomagnification of 1,1,2-TCA residues is not likely to occur.

Health Effects

1,1,2-TCA was not mutagenic when tested in Salmonella (NTP, 1985). It induced hepatocellular carcinomas and pheochromocytoma of the adrenal gland following oral exposure (78 weeks) in male and female mice but did not produce a significant increase in tumor incidence in male or female rats (NCI, 1977). EPA has classified 1,1,2-TCA according to EPA's Guidelines for Carcinogenic Risk Assessment in EPA's Group C (possible human carcinogen) based on positive evidence in mice and an absence of data on humans.

No information was found concerning the reproductive toxicity or teratogenicity of 1,1,2-TCA. No chronic studies were found other than the carcinogenesis bioassay identified above which addressed the toxicity of 1,1,2-TCA; however, single doses as low as 400 mg/kg caused liver and kidney damage in dogs. The oral LD_{50} value for 1,1,2-TCA in rats is 835 mg/kg.

Toxicity to Wildlife and Domestic Animals

The acute LC_{50} values for 1,1,2-TCA for freshwater aquatic organisms ranged from 18,000 to 81,700 ug/liter. One chronic test indicated that the acute-chronic ratio for 1,1,2-TCA was approximately 8.7. No information on the toxicity of 1,1,2-TCA to saltwater species, terrestrial wildlife, or domestic animals was available in the literature reviewed.

Regulations and Standards

Ambient Water Quality Criteria (EPA, 1986b):

The available data are not sufficient for establishing criteria. However, EPA does report the lowest values known to be toxic in aquatic organisms.

Aquatic Life (Freshwater)

Acute toxicity: 18,000 ug/liter (1,1,1-TCA and 1,1,2-TCA)
Chronic toxicity: 9,400 ug/liter

Aquatic Life (Saltwater)

Acute toxicity: No available data
Chronic toxicity: No available data

Human Health

Due to the carcinogenicity of 1,1,2-TCA, the ambient water criterion is set at zero. However, estimates of the carcinogenic risks associated with lifetime exposure from ingestion of contaminated water and aquatic organisms are:

Risk	Concentration
10^{-4}	60 ug/liter
10^{-5}	6.0 ug/liter
10^{-6}	0.6 ug/liter
10^{-7}	0.06 ug/liter

OSHA Standard (air): TWA = 45 mg/m^3 (skin)

ACGIH TLV: TWA = 55 mg/m^3 (skin)

CAG Potency Slope for oral exposure (EPA, 1990): 5.7×10^{-2} (mg/kg/day)$^{-1}$

CAG Potency Slope for inhalation exposure (EPA, 1990): 5.7×10^{-2} (mg/kg/day)$^{-1}$

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health nor pose a risk of cancer occurrence greater than a predetermined risk level.

For carcinogens such as 1,1,2-TCA, the oral and inhalation D_T values are based on the EPA Cancer Assessment Group's cancer potency slope. The cancer potency slopes have been estimated for oral exposure routes and for inhalation exposure for some chemicals. The slopes are intended to be a plausible upper bound of the potency of a carcinogen in inducing cancer at low doses. Calculation of a D_T using a cancer potency slope requires selection of an acceptable cancer risk level. A range of risk levels from 10^{-4} to 10^{-7} is considered for all carcinogens; therefore, a range of D_T values is presented. Derivation of the oral and inhalation D_T values for 1,1,2-TCA is as follows:

$$D_T = \frac{\text{Risk Level}}{\text{Potency Slope (mg/kg/day)}^{-1}}$$

$$= \frac{1 \times 10^{-4}}{5.7 \times 10^{-2} \text{ (mg/kg/day)}^{-1}}$$

The range of D_T values for 1,1,2-TCA is presented below:

Risk Level	D_T Oral Exposure (mg/kg/day)	D_T Inhalation Exposure (mg/kg/day)
10^{-4}	1.7×10^{-3}	1.7×10^{-3}
10^{-5}	1.7×10^{-4}	1.7×10^{-4}
10^{-6}	1.7×10^{-5}	1.7×10^{-5}
10^{-7}	1.7×10^{-6}	1.7×10^{-6}

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TRICHLOROETHYLENE[1]

Summary

Trichloroethylene (TCE) induced hepatocellular carcinomas in mice following oral administration and was mutagenic when tested using several microbial assay systems. Chronic inhalation exposure to high concentrations caused liver, kidney, and neurological damage and dermatological irritation in animals.

CAS Number: 79-01-6

Chemical Formula: C_2HCl_3

IUPAC Name: Trichloroethylene

Important Synonyms and Trade Names: Trichloroethylene, TCE, and ethylene trichloride

Chemical and Physical Properties

Molecular Weight: 131.5

Boiling Point: 87°C

Melting Point: -73°C

Specific Gravity: 1.4642 at 20°C

Solubility in Water: 1,100 mg/liter (Rogers et al., 1980) Table IV
825 mg/liter (Valvani et al., 1980)

Solubility in Organics: Soluble in alcohol, ether, acetone, and chloroform

Log Octanol/Water Partition Coefficient (Kow):

2.29	(Hansch and Leo, 1979)
2.29	(Rogers et al., 1980)
2.42	(Veith et al., 1983)
2.53	(Tewari et al., 1982)
3.24	(Geyer et al., 1984)
3.3	(Valvani et al., 1980)
3.3	(Davies and Dobbs, 1984)
2.38	(EPA, 1986a)

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[1] Compiled from: U.S. Environmental Protection Agency, Office of Waste Program Enforcement. September 1985b. Chemical, physical, and biological properties of compounds present at hazardous waste sites. A Final Report Prepared by Clement Associates, Inc., Arlington, Virginia.

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Soil to Water Partition Coefficient (Koc):

188	(Rogers et al., 1980) Table V (experimental)
420; 1,487	(Lyman et al., 1982) Eqn 4-8 (log Kow = 2.29; 3.30)
175; 1,073	(Lyman and Loreti, 1987) (log Kow = 2.29; 3.30)

Bioconcentration Factor:

95	(Davies and Dobbs, 1984) Eqn B (log Kow = 3)
17	(Kenaga, 1980) Table 3 (experimental)
17	(Davies and Dobbs, 1984) (Table 2) (experimental)
31.8	(Lyman et al., 1982) Eqn 5-2 (log Kow = 2.28)
32.4	(Lyman et al., 1982) Eqn 5-2 (log Kow = 2.29)
40.7	(Lyman et al., 1982) Eqn 5-2 (log Kow = 2.42)
189.7	(Lyman et al., 1982) Eqn 5-2 (log Kow = 3.3)
14	(Davies and Dobbs, 1984) Eqn A (S = 825)
27.5	(Davies and Dobbs, 1984) Eqn C (log Kow = 2.57)
52.8	(Davies and Dobbs, 1984) Eqn B (log Kow = 2.57)
52.9	(Lyman et al., 1982) Eqn 5-2 (log Kow = 2.57)

Vapor Pressure: 60 mm Hg at 20°C
57.9 mm Hg at 25°C (EPA, 1986a)

Vapor Density: 4.53

Henry's Law Constant: 1.3×10^{-2} atm-m^3/mole (calculated)
9.1×10^{-3} atm-m^3/mole (EPA, 1986a)
3.82×10^{-1} Dimensionless

Transport and Fate

Trichloroethylene (TCE) rapidly volatilizes into the atmosphere from surface waters and soil surfaces where it reacts with hydroxyl radicals to produce hydrochloric acid, carbon monoxide, carbon dioxide, and carboxylic acid. The atmospheric lifetime of TCE estimated on the basis of reactions with hydroxyl radicals is 54 hours (EPA, 1985a).

A range of experimental and estimated Kocs is reported above and indicates that some sorption of TCE to soils/sediments and dissolved organic material will occur. Pavlou (1980) estimates that sorption of volatile organic compounds will range from low to moderate. The combined water solubility and organic partitioning of TCE suggests that this compound will exhibit some degree of environmental mobility. There is evidence that microorganisms can metabolize TCE; however, it is unclear whether TCE bound to organic materials can be transformed directly or whether it must be desorbed in order to be degraded.

A range of experimental and estimated BCFs for TCE is also reported above. ASTM (1985) indicates that chemicals with BCFs less than approximately 100 have low potential for causing harm to wildlife and human health via biomagnification of residues up food chains. The magnitude of the concentration factors suggests that appreciable bioconcentration or biomagnification of TCE residues is not likely to occur.

Health Effects

TCE was mutagenic in tests using several microbial assay systems. It was carcinogenic in mice producing hepatocellular carcinomas following oral administration (NCI, 1976; NTP, 1982). TCE has been classified according to EPA's Guidelines for Carcinogenic Risk Assessment in EPA's Group B2 (probable human carcinogen), based on the finding of liver tumors in orally exposed mice and inadequate evidence in humans (EPA, 1985a).

Embryo toxicity occurred in rats exposed via inhalation to TCE at 1,800 ppm for 2 weeks prior to mating and during days 1-20 of gestation (EPA, 1985a). Inhalation for 3 weeks prior to mating and during gestation days 1-18 (rat) and during gestation days 1-21 (rabbit) also resulted in embryo toxicity. TCE has been shown to cause renal toxicity, hepatotoxicity, neurotoxicity, and dermatological reactions in animals following chronic exposure to levels greater than 2,000 mg/m^3 for 6 months (EPA, 1985a). The acute oral LD_{50} value of TCE in the rat is 4,920 and 2,402 mg/kg in the mouse.

In humans, chronic exposure is characterized by dizziness, nausea, headache, ataxia, decreased appetite, and sleep disturbances (EPA, 1985a). Effects of short-term exposure include mild eye irritation, nausea, vertigo, headache and confusion. Unconsciousness and death may occur following exposure to excessive concentrations (EPA, 1985a).

Toxicity to Wildlife and Domestic Animals

Only limited data was available on the toxicity of TCE to aquatic organisms. The acute toxicity to freshwater species was similar in the three species tested, with LC_{50} values of about 50 mg/liter (EPA, 1980). No LC_{50} values were available for saltwater species (EPA, 1980). However, 2 mg/liter caused erratic swimming and loss of equilibrium in the grass shrimp. No chronic toxicity tests were reported.

No information on the toxicity of TCE to domestic animals or terrestrial wildlife was available in the literature reviewed.

Regulations and Standards

Ambient Water Quality Criteria (EPA, 1986b):

> The available data are not adequate for establishing criteria. However, EPA does report the lowest values known to be toxic in aquatic organisms.

Aquatic Life (Freshwater)

Acute toxicity: 45 mg/liter
Chronic toxicity: 21.9 mg/liter

Aquatic Life (Saltwater)

Acute toxicity: 2 mg/liter
Chronic toxicity: No available data

Human Health

Due to the carcinogenicity of TCE, the ambient water criterion is set at zero. Estimates of the carcinogenic risks associated with lifetime exposure from ingestion of contaminated water and contaminated aquatic organisms are:

Risk	Concentration
10^{-4}	270 mg/liter
10^{-5}	27 mg/liter
10^{-6}	2.7 mg/liter
10^{-7}	0.27 mg/liter

National Primary Drinking Water Standard: 0.005 mg/liter (40 CFR Part 141).

CAG Potency Slope for Oral Exposure (EPA, 1990): 1.1×10^{-2} $(mg/kg/day)^{-1}$

CAG Potency Slope for Inhalation Exposure (EPA, 1990): 1.7×10^{-2} $(mg/kg/day)^{-1}$

NIOSH Recommended Standards (air): TWA = 100 ppm
Ceiling Level = 200 ppm
Peak Level = 300 ppm (5min/2hr)

ACGIH TLV: TWA = 50 ppm
STEL = 200 ppm

OSHA Standards (air): TWA = 100 ppm
Ceiling = 200 ppm

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health nor pose a risk of cancer occurrence greater than a predetermined risk level.

For carcinogens such as TCE, the D_T value is based on the EPA Cancer Assessment Group's cancer potency slopes. The cancer potency slopes have been estimated for oral exposure routes and for inhalation exposure for TCE. The slopes are intended to be a plausible upper bound of the potency of a carcinogen in inducing cancer at low doses. Calculation of a D_T using a cancer potency slope requires selection of an acceptable cancer risk level. A range of risk levels from 10^{-4} to 10^{-7} will be considered for all carcinogens; therefore a range of D_T values is presented. Derivation of the oral D_T values for TCE is as follows:

$$D_T = \frac{\text{Risk Level}}{\text{Potency Slope (mg/kg/day)}^{-1}}$$

$$= \frac{1 \times 10^{-4}}{1.1 \times 10^{-2} \text{ (mg/kg/day)}^{-1}}$$

$$= 9.1 \times 10^{-3} \text{ mg/kg/day}$$

The inhalation D_T values for TCE were similarly computed using inhalation potency slopes.

The range of D_T values for trichloroethylene is presented below:

Risk Level	Oral D_T (mg/kg/day)	Inhalation D_T (mg/kg/day)
10^{-4}	9.1×10^{-3}	5.9×10^{-3}
10^{-5}	9.1×10^{-4}	5.9×10^{-4}
10^{-6}	9.1×10^{-5}	5.9×10^{-5}
10^{-7}	9.1×10^{-6}	5.9×10^{-6}

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VAPONA[1]

Summary

Vapona is a member of the class of organophosphorus pesticides. The primary mode of toxicity from Vapona exposure is through inhibition of the enzyme acetylcholinesterase (ChE). Positive and negative mutagenicity results have been obtained in a variety of test systems. The NTP is currently undertaking additional studies to assess the mutagenicity and carcinogenicity of Vapona.

CAS Number: 62-73-7

Chemical Formula: $(CH_3O)_2P(O)OCH: CCl_2$

IUPAC Name: 2,2-Dichlorovinyl dimethyl phosphate

Important Synonyms and Trade Names: Dichlorvos; DDVP

Chemical and Physical Properties

Molecular Weight: 221 (Merck, 1983)

Boiling Point: 120°C at 14 mm Hg (Merck, 1983)

Specific Gravity: 1.415 (Merck, 1983)

Solubility in Water: 10,000 mg/liter (Merck, 1983)

Solubility in Organics: Miscible in aromatic hydrocarbon solvents, chlorinated hydrocarbon solvents and alcohol

Log Octanol/Water Partition Coefficient (Kow): 1.4 (Hansch and Leo, 1979)

Soil to Water Partition Coefficient (Koc):

138 (Lyman et al., 1982) Eqn 4-8 (log Kow = 1.4)
36 (Lyman and Loreti, 1987) (log Kow = 1.4)
64 (Kadeg et al., 1986) (log Kow = 1.4)

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[1] Compiled from: USAMBRDL. 1989b. Physical/Chemical and Toxicological Summaries for 62 Rocky Mountain Arsenal Contaminants. USAMBRDL. Fort Detrick, Frederick, MD.

Bioconcentration Factor:

6.8 (Lyman et al., 1982) Eqn 5-2 (log Kow = 1.4)
3.4 (Davies and Dobbs, 1984) Eqn A (S = 10,000)
7.6 (Davies and Dobbs, 1984) Eqn C (log Kow = 1.4)
11 (Davies and Dobbs, 1984) Eqn B (log Kow = 1.4)

Vapor Pressure: 1.2×10^{-2} mm Hg at 20°C (Merck, 1983)
1.0×10^{-2} mm Hg at 30°C (TDB Peer Review Committee, 1984)

Henry's Law Constant: 2.0×10^{-7} atm-m^3/mole (calculated)
2.9×10^{-7} atm-m^3/mole (calculated)
1.2×10^{-5} Dimensionless

Transport and Fate

The vapor pressure of Vapona suggests that some volatilization from environmental media is likely to occur. It is possible that released Vapona vapors will hydrolyze following reactions with atmospheric moisture and result in hydrolysis products such as desmethyldichlorvos. At acidic pHs, Vapona is more stable (i.e., more resistant to hydrolysis). For example, at 38°C and pHs of 1 or 9, the respective half-lives of Vapona are 50 and 4.5 hours (TDB Peer Review Committee, 1984). At 37.5°C and neutral pH (pH = 7) the half-life was 28 hours. The likely primary hydrolysis product--desmethyl dichlorvos--may further hydrolyze to chlorofenvinphos (Supona) (USAMBRDL, 1985). Cogley and Foy (1978) indicate a half-life of less than one month for Vapona.

A range of estimated Kocs is reported above and indicates that some sorption of Vapona to soils/sediments and dissolved organic material will occur. The combined water solubility and low organic partitioning suggest that Vapona will exhibit some degree of environmental mobility.

A range of estimated BCFs is also reported above. ASTM (1985) indicates that chemicals with BCFs less than approximately 100 have low potential for causing harm to wildlife and human health via biomagnification of residues up food chains. The magnitude of the concentration factors suggests that appreciable bioconcentration or biomagnification of Vapona residues is not likely to occur.

Health Effects

The primary mode of toxicity of Vapona in humans and animals is through inhibition of the enzyme acetylcholinesterase (ChE) in the central and peripheral nervous systems. Symptoms of exposure include headache, blurred vision, constricted pupils, chest tightness, salivation, sweating, muscular weakness, tremors, and convulsions with death occurring (at very high doses) from respiratory failure (Shell Internationale, 1981). Men exposed for 30-60 minutes to Vapona concentrations up to 6.9 mg/m^3 exhibited no clinical effects or inhibition of blood ChE activity (Shell Internationale, 1981). Groups of five men received

total oral doses of 1.0, 1.5, 2.0, or 2.5 mg/day Vapona divided over two gelatin capsules for 28 days. Another group received 1.5 mg/day for 60 days. The 2.5 mg/day dose groups experienced decreases in plasma ChE activity beginning the second week. When plasma ChE levels showed a 30 percent decrease (20 days), the dosing was discontinued. The 2.0 mg/day dose also produced a reduction in plasma ChE during the second week of dosing, which reached a maximum of 29 percent two days following the last dose. The 1.5 mg/day dose group (28-day exposure) exhibited no change in plasma ChE, while those in the 60-day study exhibited reduced plasma ChE (27 percent). The 1.0 mg/day group also exhibited no change in plasma ChE levels. A subchronic oral toxicity study in rats exposed to diets containing 0, 5, 20, 200, 500, or 1,000 ppm Vapona resulted in decreased plasma ChE activity at all dose levels as compared with controls. Levels of ChE gradually returned to normal levels except in the 200 ppm and higher dose groups. Erythrocyte ChE was also decreased in the 200 ppm and higher dose groups (Shell Internationale, 1981). In another study, rats fed Vapona for 15 weeks in their diet (0, 0.1, 1.0,10, 100, or 1,000 ppm) displayed no signs of toxicity. Rats in the highest dose group exhibited decreased growth rates at the beginning of the study and marked inhibition of ChE activity in plasma, erythrocytes and brains. Females in the 10 and 100 ppm groups also displayed reduced levels of plasma and erythrocyte ChE activity (Shell Internationale, 1981).

Rats chronically exposed (2 years) to 0.047, 4.67, 46.7, or 234 ppm Vapona displayed no signs of intoxication. No effects were observed on behavior, mortality rate, weight gain, food consumption, terminal body and organ weights, hematology, urinalysis, or tumor incidence (Shell Internationale, 1981). Plasma and erythrocyte ChE were depressed throughout the study in the two high-dose groups. Brain ChE activity was depressed only in the highest group. Histological examination revealed hepatocellular vacuolization in the high-dose group, and in most females and some males, at 46.7 ppm. The identified NOEL in this study was 4.7 ppm. No carcinogenic effects were noted in the study (Shell Internationale, 1981). In another chronic study, dogs exposed to Vapona in their diets (0.09, 0.32, 3.2, 32.0, or 256 ppm) exhibited no differences in survival, weight gain, food consumption, hematology, or urinalysis. Plasma ChE was decreased at the two highest doses and erythrocyte ChE activity was depressed at 3.2 ppm and above. It was concluded that 0.32 ppm was the NOEL for this study.

Positive indications of mutagenicity have been observed following Vapona treatment in Aspergillus nidulans (point mutations, cross-overs), Chinese hamster fibroblast lung cells (breaks, translocations, rings, gaps), and Chinese hamster V79 cells (sister chromatid exchange) (Shell Internationale, 1981). Positive results were also obtained by the NTP with L5178Y mouse lymphoma cells (NTP, 1985). Vapona has also tested positive for cytogenetic effects in Chinese hamster ovary cells (NTP, 1986). Negative results were obtained following Vapona treatment in Drosophila melanogaster (Shell Internationale, 1981). Dominant lethal assays in mice, cytogenetic studies on bone marrow and spermatogonia in mice and Chinese hamsters as well as host-mediated assays, have all been negative (Shell Internationale, 1981). Vapona has tested positive for mutagenicity in Salmonella (EPA, 1990).

Male mice treated with Vapona at 40 mg/kg-day by gavage in a two-year NTP study did exhibit a statistically significant increase in the incidence of squamous papillomas of the fore stomach (EPA, 1990). A significant positive trend was also observed in dosed females (EPA, 1990). Another two-year (NTP) study (gavage) with rats indicated a positive dose related trend in the incidence of pancreatic acinaradenoma and alveolar/bronchial adenoma in treated males (EPA, 1990). Statistically significant elevations in the incidence of leukemia (lymphocytic, monocytic, mononuclear, or undifferentiated) were also observed in male rats (EPA, 1990). Vapona has been classified in Group B2 according to EPA's Guidelines for Carcinogen Risk Assessment.

No teratogenic effects were observed following Vapona exposure in rabbits during days 6-18 of gestation, nor in rats or mice dosed during gestation (Shell Internationale, 1981). No reproductive effects were noted in a 3 generation study in rats fed 0.1, 1.0, 10, 100, or 500 ppm Vapona. However, rabbits given 5 mg/kg orally during days 6-18 of gestation exhibited an increased number of resorptions (USAMBRDL, 1985).

The acute oral toxicity values (LD_{50}) for Vapona in male and female rats are 80 and 56 mg/kg, respectively (USAMBRDL, 1985).

Toxicity to Wildlife and Domestic Animals

Cows fed grain which contained 20 ppm Vapona for eight days exhibited no signs of toxicity or depression of ChE activity (Shell Chemical Company, 1965). However, at concentrations of 100 and 200 ppm a slight depression of erythrocyte ChE was observed after eight days, while at 500 and 2,000 ppm severe depression of erythrocyte ChE was observed at 8 days (Shell Chemical Company, 1965).

Acute toxicity data are available for avian species. Acute oral LD_{50} values for pheasants (Phasianus colchicus), mallard ducks (Anas platyrhynchos), starlings (Sturnus vulgaris), and redwing blackbirds (Anglaius phoeniceus) are 9.0, 7.8, 12, and 17 mg/kg, respectively (Shell Internationale, 1981).

The acute toxicity of Vapona to freshwater fish has been evaluated. The 96 hr LC_{50} values for cutthroat trout (Salmo clarki), lake trout (Salvelinus namaycush), bluegills (Lepomis macrochirus), and fathead minnows (Pimephales promelas) are 0.17, 0.19, 0.9, and 12 mg/l, respectively (Shell Internationale, 1981).

The acute oral toxicity of Vapona (LD_{50}) in rabbits is 12.5 mg/kg and approximately 100-300 mg/kg in the dog (USAMBRDL, 1985).

Regulations and Standards

OSHA PEL: TWA = 1 mg/m^3 (skin)

ACGIH TLV: TWA = 0.90 (skin)

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health nor pose a risk of cancer occurrence greater than a predetermined risk level.

For carcinogens such as Vapona, the D_T value is based on the EPA Cancer Assessment Group's cancer potency slopes. The potency slopes have been developed for oral exposure routes and for inhalation exposures for some chemicals. The potency slopes are intended to be a plausible upper bound of the potency of a carcinogen in inducing cancer at low doses.

Calculation of a D_T using a cancer potency slope requires selection of an acceptable cancer risk level. A range of risk levels from 10^{-4} to 10^{-7} is considered for all carcinogens, therefore a range of D_T values is presented. Derivation of the D_T values for Vapona is as follows:

$$D_T = \frac{\text{Risk Level}}{\text{Potency Slope (mg/kg-day)}^{-1}}$$

$$= \frac{1 \times 10^{-4}}{0.29 \text{ (mg/kg-day)}^{-1}}$$

$$= 3.4 \times 10^{-4} \text{ mg/kg/day}$$

The range of D_T values for Vapona is presented below:

Risk Level	Oral D_T (mg/kg/day)	Inhalation D_T (mg/kg/day)
10^{-4}	3.4×10^{-4}	3.4×10^{-4}
10^{-5}	3.4×10^{-5}	3.4×10^{-5}
10^{-6}	3.4×10^{-6}	3.4×10^{-6}
10^{-7}	3.4×10^{-7}	3.4×10^{-7}

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XYLENES (o,m,p)[1]

Summary

Xylene has been shown to be fetotoxic in rats and mice. In humans, exposure to high concentrations of xylene adversely affects the central nervous system and irritates the mucous membranes. Prolonged exposure to high concentrations can cause severe lung congestion and intra-alveolar hemorrhage.

Xylene has three isomers, o-, m-, and p-xylene. They generally have similar chemical and biological characteristics and therefore will be discussed together.

CAS Number:

Mixed Xylene:	1330-20-7
m-Xylene:	109-38-3
o-Xylene:	95-47-6
p-Xylene:	106-42-3

Chemical Formula: $C_6H_4(CH_3)_2$

IUPAC Name: Dimethylbenzene

Important Synonyms and Trade Names:

Mixed Xylene:	Dimethylbenzene, xylol
m-Xylene:	1,3-Dimethylbenzene, m-xylol
o-Xylene:	1,2-Dimethylbenzene, o-xylol
p-Xylene:	1,4-Dimethylbenzene, p-xylol

Chemical and Physical Properties

Molecular Weight: 106.17

Boiling Point:

Mixed Xylene:	137-140°C
m-Xylene:	139°C
o-Xylene:	144°C
p-Xylene:	138°C

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[1] Compiled from: U.S. Environmental Protection Agency, Office ofWaste Program Enforcement. September 1985. Chemical, physical, and biological properties of compounds present at hazardous waste sites. A Final Report Prepared by Clement Associates, Inc., Arlington, Virginia.

Also: USAMBRDL. 1985. Physical/Chemical and Toxicological Summaries for 62 Rocky Mountain Arsenal Contaminants. USAMBRDL. Fort Detrick, Frederick, MD.

Melting Point:

m-Xylene:	-48°C
o-Xylene:	-25°C
p-Xylene:	13°C

Specific Gravity: 0.86

Solubility in Water: 130 mg/liter at 25°C [m-xylene] (EPA, 1986)
175 mg/liter at 25°C [o-xylene] (Sax, 1986)
198 mg/liter at 25°C [p-xylene] (Sax, 1986)
198 mg/liter (mixed) (EPA, 1986)

Solubility in Organics: Soluble in alcohol, ether, and other organic solvents

Log Octanol/Water Partition Coefficient (Kow):

o-xylene:	2.77 (Moriguchi, 1975)
	2.95 (Valvani et al., 1980)
	3.13 (Tewari et al., 1982) Table I
p-xylene:	3.15 (Valvani et al., 1980; Moriguchi, 1975)
	3.18 (Tewari et al., 1982)
m-xylene:	3.20 (Valvani et al., 1980; Tewari et al., 1982; Moriguchi, 1975)
	3.26 (EPA, 1986) Mixed isomers

Soil to Water Partition Coefficient (Koc):

[o-, p-, m-isomers:]

1,157; 1,414	(Lyman et al., 1982) Eqn 4-8 (log Kow = 3.10; 3.26)
750; 999	(Lyman and Loreti, 1987) (log Kow = 3.10; 3.26)

Bioconcentration Factor:

95	(Davies and Dobbs, 1984) Eqn B (log Kow = 3)
56	(Davies and Dobbs, 1984) Eqn C (log Kow = 3)
34.7	(Davies and Dobbs, 1984) Eqn A (S = 165)
75	(Lyman et al., 1982) Eqn 5-2 (log Kow = 2.77)
134	(Lyman et al., 1982) Eqn 5-2 (log Kow = 3.10)
146	(Lyman et al., 1982) Eqn 5-2 (log Kow = 3.15)
159	(Lyman et al., 1982) Eqn 5-2 (log Kow = 3.20)
8.7	(Davies and Dobbs, 1984) Eqn A (log Kow = 3.10)
109	(Davies and Dobbs, 1984) Eqn B (log Kow = 3.10)
51.4	(Davies and Dobbs, 1984) Eqn C (log Kow = 3.10)

Vapor Pressure: 10 mm Hg at 25°C

Vapor Density: 3.7

Flash Point: 25°C (closed cup)

Henry's Law Constant: 5.6×10^{-4} atm-m^3/mole (calculated)
7.04×10^{-3} atm-m^3/mole (EPA, 1986)

Transport and Fate

Volatilization and subsequent photooxidation by reaction with hydroxyl radicals in the atmosphere are important transport and fate processes for xylene occurring in the upper layer of soil and in aquatic environments. Products of the hydroxylation reaction include carbon dioxide, peroxyacetylnitrate (PAN), and cresol. A range of estimated Kocs is reported above and indicates that sorption of xylenes to soil/sediment and dissolved organic material will occur. Pavlou (1980) estimates that sorption of volatile organics will range from low to moderate. The combined water solubility and organic partitioning indicate that xylene and its isomers will exhibit some degree of environmental mobility. Biodegradation is also an important fate process in both soils and the aquatic environment. Xylenes have been shown to persist for up to 6 months in soil. Because of their low water solubility high octanol/water partition coefficient and rapid biodegradation, xylenes are unlikely to leach rapidly into groundwater in high concentrations.

A range of estimated BCFs for xylenes is also reported above. ASTM (1985) indicates that chemicals with BCFs less than approximately 100 have low potential for causing harm to wildlife and human health via biomagnification of residues up food chains. The magnitude of the concentration factors suggests that some bioconcentration of xylene residues may occur.

Health Effects

The NTP has recently conducted oral toxicity tests with mixed xylenes in rats and mice to determine carcinogenicity. Groups of 50 rats of each sex were administered doses of 0, 250, or 500 mg/kg xylenes by gavage 5 days/week for 103 weeks in a carcinogenicity test (NTP, 1986). Groups of 50 mice of each sex were administered 0, 500, or 1,000 mg/kg xylenes on the same schedule. At no site was the incidence of nonneoplastic or neoplastic lesions in dosed rats or mice of either sex considered to be related to the administration of xylenes (NTP, 1986). Survival rates of male rats were dose related (e.g., vehicle control survival, 36/50; low-dose, 26/50; and high-dose 20/50). Most of the deaths were gavage related. Body weights of high-dose males were slightly lower (5-8 percent) than those of controls after week 59. Mean body weights of low-dose and control male rats and dosed (all levels) and control female rats were comparable. Survival rates of female rats and both sexes of dosed mice were not significantly different from controls. Mixed xylenes (o, m, p-xylene, or ethylbenzene) were not mutagenic when tested with or without metabolic activation in several Salmonella typhimurium strains (NTP, 1986).

Xylene is not teratogenic but has caused fetotoxicity in exposed rats and mice. Acute exposure to high levels of xylene affects the central nervous system and irritates the mucous membranes. Aged rats were exposed to a single concentration of xylene (200 ppm) in their diets for up to six months in a study by Bowers et al. (1982). No gross or light microscopic effects were seen. The administered concentration was considered a NOAEL because ultrastructural changes in liver morphology which did not appear to be adverse were noted (EPA, 1984). Weaknesses of the study include the use of aged animals, a lack of chemical stability monitoring, the use of a single exposure level and a lack of examination of other tissues. The oral LD_{50} value of xylene in rats is 4,300 mg/kg (NIOSH, 1983). The inhalation LC_{50} value (4 hr) in rats is 5,000 ppm (NIOSH, 1983).

Toxicity to Wildlife and Domestic Animals

Xylene adversely affected adult trout at concentrations as low as 3.6 mg/liter in a continuous flow system. Juvenile trout avoided xylene at concentrations greater than 0.1 mg/liter. The LC_{50} in adult trout was determined to be 13.5 mg/liter. The LC_{50} values for other freshwater fish were approximately 30 mg/liter in a static system. [Note: This test likely underestimated toxicity because the concentration in the water column available for uptake is not constant.] Only a few studies have been done on the toxicity of xylene to saltwater species. These indicated that the m- and o-xylene isomers have similar toxicities and are probably less toxic than p-xylene, and that saltwater species are generally more susceptible than freshwater species to the detrimental effects of xylene (LC_{50} = 10 mg/liter for m- and o-xylene and LC_{50} = 2 mg/liter for p-xylene). However, these generalizations are based on limited data.

No information on the toxicity of xylenes to terrestrial wildlife and domestic animals was available in the literature reviewed. However, because of the low acute toxicity of xylenes and the high volalility, it is unlikely that they would be encountered in concentrations which would be toxic to wild or domestic birds or mammals.

Regulations and Standards

NIOSH Recommended Standards (air): TWA = 435 mg/m^3
Ceiling Level = 870 mg/m^3 (10 min)

ACGIH: TWA = 434 mg/m^3
STEL = 651 mg/m^3

OSHA Standard (air): TWA = 435 mg/m^3
STEL = 655 mg/m^3

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health nor pose a risk of cancer occurrence greater than a predetermined risk level.

For xylenes, the oral D_T value is based on the current RfD (EPA, 1990a). The RfD is based on a chronic (2 year) gavage study in rats. A NOAEL of 250 mg/kg/day was identified based on hyperactivity, decreased body weight and increased mortality. An UF of 100 was incorporated to address the extrapolation of results to humans (10) and intraspecies variability (sensitive subgroups) (10). Derivation of the oral D_T value is as follows:

$$D_T = \frac{\text{NOAEL (mg/kg/day)}}{\text{UF}}$$

$$= \frac{250}{100}$$

= 2.5 mg/kg/day [Note: EPA has rounded the RfD to 2.0 mg/kg/day in their derivation.]

The inhalation D_T for xylene is based on the RfD specified in the EPA HEAST (EPA, 1990b). The RfD is derived from a subchronic inhalation study in humans. Though details of the study were not available, the toxicological effect of concern was central nervous system effects, and nose and throat irritation (EPA, 1990b). An UF of 100 was incorporated by EPA to address intraspecies variability (i.e., sensitive subgroups) (10), and the use of LOEL (10).

The LOEL identified from the study was 27 mg/m^3. The corresponding reference concentration computed after incorporation of the UFs is 0.3 mg/m^3 (EPA, 1990b). Derivation of a RfD in mg/kg-day was achieved assuming a reference daily breathing rate of 20 m^3 for a 70 kg adult. The resulting inhalation reference dose for xylene is 8.6×10^{-2} mg/kg/day.

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ZINC[1]

Summary

Ingestion of excessive amounts of zinc can cause fever, vomiting, and stomach cramps. Exposure to high concentrations of zinc oxide fumes can cause metal fume fever. Inhalation of mists or fumes may irritate the respiratory tract, and contact with zinc chloride may irritate the eyes and skin. High levels of zinc in the diet have been shown to retard growth and produce defective mineralization of bone. Zinc generally exists in nature as a salt with a valence of +2.

CAS Number: 7440-66-6

Chemical Formula: Zn

IUPAC Name: Zinc

Chemical and Physical Properties:

Atomic Weight: 65.38

Boiling Point: 907°C

Melting Point: 419.58°C

Specific Gravity: 7.133 at 25°C

Solubility in Water: Insoluble; some salts are soluble

Solubility in Organics: Soluble in acid and alkali

Vapor Pressure: 1 mm Hg at 487°C

Transport and Fate

Zinc can occur in both suspended and dissolved forms. Dissolved zinc may occur as the free (hydrated) zinc ion or as dissolved complexes and compounds with varying degrees of stability and toxicity. Suspended (undissolved) zinc may be dissolved following minor changes in water chemistry or may be sorbed to suspended matter. The predominant fate of zinc in aerobic aquatic systems is sorption of the divalent cation by hydrous iron and manganese oxides, clay minerals, and organic material. The efficiency of these materials in removing zinc from solution varies according to their compositions and concentrations, the

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[1] Compiled from: U.S. Environmental Protection Agency, Office of Waste Program Enforcement. September 1985. Chemical, physical, and biological properties of compounds present at hazardous waste sites. A Final Report Prepared by Clement Associates, Inc., Arlington, Virginia.

pH and salinity of the water, the concentrations of complexing ligands, and the concentration of zinc. Concentrations of zinc in suspended and bed sediments always exceed concentrations in ambient water. In reducing environments, precipitation of zinc sulfide limits the mobility of zinc. However, under aerobic conditions, precipitation of zinc compounds is probably important only where zinc is present in high concentrations. Zinc tends to be more readily sorbed at higher pH than lower pH and tends to be desorbed from sediments as salinity increases. Compounds of zinc with the common ligands of surface waters are soluble in most neutral and acidic solutions, so that zinc is readily transported in most unpolluted, relatively organic-free waters.

The relative mobility of zinc in soil is determined by the same factors affecting its transportation in aquatic systems. Atmospheric transport of zinc is also possible. However, except near sources such as smelters, zinc concentrations in air are relatively low and fairly constant.

Since it is an essential nutrient, zinc is bioaccumulated even in the absence of abnormally high ambient concentrations. Zinc does not appear to be biomagnified. Although zinc is actively bioaccumulated in aquatic systems, the biota appear to represent a relatively minor sink compared to the sediments. Zinc is one of the most important metals in biological systems. Since it is actively bioaccumulated, the environmental concentrations of zinc probably exhibit seasonal fluctuations.

Health Effects

Testicular tumors have been produced in rats and chickens when zinc salts are injected intratesticularly, but not when other routes of administration are used (EPA, 1984). Zinc may be indirectly important with regard to cancer since its presence seems to be necessary for the growth of tumors. Laboratory studies suggest that although zinc-deficient animals may be more susceptible to chemical induction of cancer, tumor growth is slower in these animals (EPA, 1984). There is no evidence that zinc deficiency has any etiological role in human cancer. There are no data available to suggest that zinc is mutagenic or teratogenic in animals or humans (EPA, 1984).

Zinc is an essential trace element that is involved in enzyme functions, protein synthesis, and carbohydrate metabolism (EPA, 1984). Ingestion of excessive amounts of zinc may cause fever, vomiting, stomach cramps, and diarrhea. Fumes of freshly formed zinc oxide can penetrate deep into the alveoli and cause metal fume fever (EPA, 1984). Zinc oxide dust does not produce this disorder. Contact with zinc chloride can cause skin and eye irritation. Inhalation of mists or fumes may irritate the respiratory and gastrointestinal tracts. Zinc in excess of 0.25 percent in the diet of rats causes retardation, hypochromic anemia, and defective mineralization of bone (EPA, 1984). No zinc toxicity is observed at dietary levels below 0.25 percent.

Studies with animals and humans indicate that metabolic changes may occur due to the interaction of zinc and other metals in the diet. Exposure to cadmium can cause changes in the distribution of zinc, with increases in the liver and kidneys (organs where cadmium

also accumulates). Excessive intake of zinc may cause copper deficiencies and result in anemia. Interaction of zinc with iron or lead may also lead to changes that are not produced when the metals are ingested individually. EPA has classified zinc in Group D (not classificable) according to the Guidelines for Carcinogenic Risk Assessment.

Toxicity to Wildlife and Domestic Animals

Zinc produces acute toxicity in freshwater organisms over a range of concentrations from 90 to 58,100 ug/liter and appears to be less toxic in harder water (EPA, 1980). Acute toxicity is similar for freshwater fish and invertebrates (EPA, 1980). Chronic toxicity values range from 47 to 852 ug/liter and appear to be relatively unaffected by hardness (EPA, 1980). A final acute-chronic ratio for freshwater species of 3.0 has been reported. Although most freshwater plants appear to be insensitive to zinc, one species, the alga Selenastrum capricornutum, exhibited toxic effects at concentrations from 30 to 700 ug/liter (EPA, 1980). Reported acute toxicity values range from 2,730 to 83,000 ug/liter for saltwater fish and from 166 to 55,000 ug/liter for invertebrate saltwater species (EPA, 1980). Zinc produces chronic toxicity in the mysid shrimp at 166 ug/liter. The final acute-chronic ratio for saltwater species is 3.0. Toxic effects are observed in saltwater plant species at zinc concentrations of 50 to 25,000 ug/liter (EPA, 1980).

Zinc poisoning has occurred in cattle. In one outbreak, poisoning was caused by food accidentally contaminated with zinc at a concentration of 20 g/kg. An estimated intake of 140 g of zinc per cow per day for about 2 days was reported. The exposed cows exhibited severe arthritis, and some died or had to be slaughtered. Postmortem findings showed severe pulmonary emphysema with changes in the myocardium, kidneys, and liver. Zinc concentrations in the liver were extremely high. Based on relatively limited data, some researchers have speculated that exposure to excessive amounts of zinc may constitute a hazard to horses. Laboratory studies and findings in foals living near lead-zinc smelters suggest that excessive exposure to zinc may produce bone changes, joint afflictions, and lameness. In pigs given dietary zinc at concentrations greater than 1,000 mg/kg, decreased food intake and weight gain were observed. At dietary levels greater than 2,000 mg/kg, deaths occurred as soon as 2 weeks after exposure; severe gastrointestinal changes and brain damage, both of which were accompanied by hemorrhages, were observed, as well as changes in the joints. High concentrations of zinc were found in the liver in these same studies.

Regulations and Standards

Ambient Water Quality Criteria (EPA, 1986):

Aquatic Life (Freshwater)

Acute toxicity: $e^{[0.8473\ln(\text{hardness})+0.884]}$ ug/liter
Chronic toxicity: 47 ug/liter

At hardnesses of 50, 100, and 200 mg/liter $CaCO_3$, the acute criteria are 180, 320, and 570 ug/liter.

Aquatic Life (Saltwater)

Acute toxicity: 170 ug/liter
Chronic toxicity: 58 ug/liter

Human Health

Organoleptic criterion: 5 mg/liter

ACGIH TLV:	Zinc chloride fume:	TWA = 1 mg/m^3
		STEL = 2 mg/m^3
	Zinc oxide fume:	TWA = 5 mg/m^3
		STEL = 10 mg/m^3
	Zinc oxide dust:	TWA = 10 mg/m^3 (nuisance particulate)

NIOSH Recommended Standard: 5 mg/m^3 (zinc oxide)

OSHA Standard: TWA = 10 mg/m^3 (zinc oxide total dust)
5 mg/m^3 (zinc oxide respirable fraction)

D_T Value

The oral D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health nor pose a risk of cancer occurrence greater than a predetermined risk level.

The oral D_T value for zinc is based on the same data used by EPA to generate the acceptable chronic intake value for oral exposure (EPA, 1984). The human data which have been used as a basis for this value are case reports of the therapeutic use of zinc to accelerate the healing of ulcers and arthritis and to aid recovery of sickle cell anemia patients. Oral dosages of encapsulated zinc approximating a total daily dose of 150 mg/day were administered (2.14 mg/kg/day assuming a 70 kg human weight). No adverse effects were noted. Therefore, this dose was chosen as a human median effective dose (MED) from which to derive an acceptable oral chronic intake. An UF of 10 is employed to protect sensitive human populations. Derivation of the oral D_T for zinc is computed as follows:

$$D_T = \frac{\text{MED (mg/kg/day)}}{\text{UF}}$$

$$= \frac{2.14}{10}$$

$$= 0.214 \text{ mg/kg/day}$$

The inhalation D_T value for zinc is based on the TLV for zinc chloride set forth by the ACGIH (1989) and used by EPA as a basis for the AIC for zinc (EPA, 1984). The TLV of 1 mg/m^3 is multiplied by an eight-hour inhalation rate of 10 m^3/day, and by a factor of five days/seven days to adjust the exposure duration. This value is divided by 70 kg, the reference body weight for an adult, to yield a dose of 0.14 mg/kg/day. An UF of 10 is used in deriving the D_T for zinc to address sensitive subgroups. This yields a D_T (AIC) of 0.01 mg/kg/day.

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